VOL. XXXI. NO. 1 NOVEMBER, 1937

PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

LONGMANS, GREEN & Co LTD
39, PATERNOSTER ROW, LONDON
NEW YORK · BOMBAY · CALCUTTA · MADRAS

Proceedings of the Royal Society of Medicine Vol. XXXI 1

Section of Epidemiology and State Medicine

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[*October* 22, 1937]

The Epidemiology of Encephalitis Lethargica

PRESIDENT'S ADDRESS

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> "However, the Mercy of God hath scattered the great heap of Diseases, and not loaded one Country with all: some may be new in one country which have been old in another. New discoveries of the Earth discover new Diseases: for besides the common Swarm, there are endemial and local Infirmities proper unto certain Regions, which in the whole Earth make no small Number: and if Asia, Africa and America should bring in their List, Pandora's Box would swell, and there must be a strange Pathology."

Thus Sir Thomas Browne in a *Letter to a Friend*. His words may aptly serve as my text to these remarks on the epidemiology of encephalitis lethargica.

PAST APPEARANCES OF ENCEPHALITIS LETHARGICA

When encephalitis lethargica appeared in this country in 1918, its advent was sudden, "a blast from the stars", as Willis might have termed it. To all intents and purposes we were faced with a new disease, whose pathology, clinical features, and epidemiology had to be worked out *de novo*. Owing to war conditions then prevailing, we were not aware until later of the description given by von Economo of the disease which had appeared the year previously (1917) in Vienna. There was also an outbreak of obscure disease in Roumania in 1915, which Marinesco subsequently regarded as one of encephalitis lethargica. Later the medical historians searched into the annals of the past and produced examples of similar outbreaks of disease of the central nervous system associated with lethargy. There is the "lethargus" accompanied by fever of Hippocrates, Coelius Aurelianus, and Aretaeus of Cappadocia. Netter doubted this identification with encephalitis. von Economo quoted a record of a "Schlafkrankheit" epidemic in the year 1580, which affected nearly the whole of Europe. Sydenham described an epidemic which he called *febris comatosa*, on account of sleepiness being a prominent symptom. This prevailed in London from 1673 to 1675. The symptoms resemble those of encephalitis lethargica and hiccup is noted among them. Ebstein (1921) considers that this is probably the first account of an epidemic of encephalitis lethargica which we possess. In 1695 Albrecht of Hildesheim described a sporadic somnolent ophthalmoplegic form, an isolated case. The Tübingen outbreak of 1712, frequently called "sleeping sickness" through a misquotation from the original account by Camerarius, does not appear to have been lethargic in nature. In 1745 Ozanam mentioned in his *Histoire des Maladies Épidémiques* a sleeping epidemic, and in 1763 Lepecq de la Clôture is said to have described a "coma somnolentum" in Rouen. Chorea electrica, as described by Dubini in 1846, may be identical with the myoclonic form of encephalitis. From 1890 to 1891 an epidemic somnolence prevailed in Italy termed "nona". This followed on the pandemic of influenza (1889 to 1890) during which cases with cerebral symptoms arose, equally suggestive of encephalitis lethargica.

In addition, isolated cases have occurred which in the light of later knowledge are recognizable as examples of this disease. A. J. Hall (1924) saw a boy aged 11, in 1903, with lethargic symptoms, and Nixon, at Bristol in 1908, saw a typical case which terminated in paralysis agitans.

Care must naturally be observed in regard to the identification of encephalitis lethargica in these historical accounts. The consensus of evidence is that encephalitis

lethargica has occurred before, but has only since 1917 been recognized as a pathological entity, being first described by von Economo.

The Increasing Incidence of Epidemic Nervous Diseases

It is naturally interesting to speculate as to why encephalitis lethargica reappeared among us in epidemic form and rapidly became so prevalent that in a comparatively short time outbreaks were reported from all quarters of the globe. One cause, indubitably, is the increased subjection of the human central nervous system to attacks of epidemic disease. I devoted one of my Milroy Lectures in 1925 to this subject. In it I dwelt upon the appearance of outbreaks of cerebrospinal meningitis on a scale of severity previously unknown in this country (this disease still prevails and there was a high incidence of it in England and Wales in 1931), the prevalence of epidemics of poliomyelitis since 1897, and the advent of encephalitis lethargica. Even this high epidemic prevalence is not the whole story. There are, as we shall consider presently, several forms of epidemic encephalitis; an increased number of cases of encephalitis have been recorded in recent years as sequelæ of the acute infectious diseases, e.g. measles and scarlet fever; post-vaccinal encephalitis has proved a serious problem since 1922, and from time to time outbreaks of obscure nervous disease are reported which fit into no recognized nosological classification.

In the lecture to which I have referred, several possible explanations, not necessarily incompatible, for this increased frequency of epidemic nervous diseases, were discussed.

Modern methods of transportation, for instance, bring individuals in contact with one another much more frequently than formerly. Infection may thus travel with the speed of modern transport from one country to another, or from one part of the same country to another. The increase of large towns, the tendency of urban populations to assemble in crowded gatherings, enhance the opportunities for personal infection, and a disease which in the eighteenth or nineteenth centuries might have been sporadic or endemic becomes epidemic or pandemic in the twentieth century. The movements of troops to and fro in all parts of the world during the war favoured outbreaks of influenza and cerebrospinal meningitis. At the same time I pointed out this could not be the whole explanation, for both cerebrospinal fever and poliomyelitis had been increasing in frequency and assuming epidemic form prior to the war, whilst the increase in encephalitis lethargica, subsequently to the war years, possibly implied an increasing susceptibility of nervous tissues to infection.

We may further speculate as to whether epidemic diseases of the central nervous system occur in epidemic cycles, as do influenza and other infectious diseases. The historical evidence for encephalitis lethargica, which we have considered, implies that the *materies morbi* of the disease must have been present in the world for centuries. For the initiation of an epidemic wave it may be surmised that several factors come into play from time to time, which, either by increasing the virulence of the causal virus, or by lowering the defensive forces of the human organism, or by the exercise of both influences, bring about an epidemic.

It is also well not to forget the question of the soil in considering the seed. It is a truism of medicine that a disease is prone to attack an individual at the weakest or most fatigued point of bodily resistance. To this rule the central nervous system is no exception. Hughlings Jackson long ago pointed out that study of the individual patient comes before the study of the disease, for a disease is rarely typical, but is modified by the characteristics of the patient. The environmental conditions under which the human nervous system functions to-day have been considerably modified by so-called modern progress; the system itself is subjected to more frequent and urgent stimuli than formerly. Fatigued or overworked tissues of the central nervous system may be thereby rendered more susceptible to the attacks of invading organisms. Encephalitis lethargica has an epidemic seasonal prevalence, so that cosmic influences, to which the epidemiologists of the seventeenth and eighteenth centuries paid much attention, should not be overlooked. There is also the possible

evolution of new organisms affecting the central nervous system. This may have occurred in one of the following ways : (*a*) originally harmless parasites of man may have assumed inimical characteristics, in the struggle for existence ; (*b*) they may have been organisms causing catarrh of the nasopharynx or gastro-intestinal tract which now tend to affect the brain and spinal cord. The catarrhal forms seen in the abortive or mild types of encephalitis lethargica or poliomyelitis afford some support for this view ; (*c*) the organisms may resemble the pneumococcus in being widespread amongst human beings and capable, under certain conditions, of giving rise to antigenic infection ; (*d*) they may have been saprophytes in nature but are now assuming the role of human parasites. Of this we have no evidence. Investigations into epidemic nervous disease in animals have afforded no substantial evidence that the increasing incidence of epidemic nervous disease is due to the transmission of epizootic organisms to man. It is true that Mr. L. P. Pugh, F.R.C.V.S. (1926) reported an outbreak of epidemic encephalitis in dogs which occurred at Sevenoaks, March to July 1926. There were a definite number of lethargic cases, and over 50 cases were fatal. Mr. Pugh considered that both in symptomatology and in the character of the cerebral lesions this canine disorder was almost identical with human encephalitis lethargica. It is of course possible that the virus may simultaneously affect man and animals in epidemic form.

Our discussion proves to be a philosophical exercise, for none of the speculations advanced as to the advent of encephalitis lethargica is capable of scientific proof. We have still much to learn about the laws which initiate outbreaks of epidemic disease. Greenwood and Topley's researches (1936) into experimental epidemiology are teaching us the elements of the subject. Their evidence that an outbreak of disease may be initiated by the evolution or importation of an "epidemic strain" of the causative organism bears upon the problem of the appearance of encephalitis lethargica in epidemic form.

Encephalitis Lethargica and the Epidemic Constitution

I shall not delay here to discuss whether epidemiologically, encephalitis lethargica is part of the "epidemic constitution" of influenza, a thesis which was so ably advocated by that great epidemiologist, Sir William Hamer (1928) whose recent death we all deplore. The subject has been discussed repeatedly before this Section, and I have shown elsewhere that in their manner of invasion, symptomatology, courses and complications, influenza and encephalitis lethargica are quite distinct, and in their epidemic behaviour there are striking differences. This statement, as Professor Greenwood (1935) points out, would probably have been accepted by Hamer and his disciple Crookshank as correct. The whole contention is that the different forms of epidemic nervous diseases are not influenza but part of its setting, "trailers", which sometimes precede and sometimes follow the outbreak of influenza.

The recent epoch-making researches of Smith, Laidlaw, and Andrewes (1933, 1935) have solved the problem of the ætiology of influenza by demonstrating that a filtrable virus will transmit the disease to ferrets. It also appears that different strains of the virus seem to be responsible for different clinical forms of influenza, and this is supported by the specificity of the immunological reactions observed.

Influenza becomes thus more clearly defined as a clinical entity, and, in the light of this knowledge, it seems even still more unwise to assume that all cases of disease occurring in the course of a widespread epidemic of influenza are necessarily an integral part of the epidemic. Otherwise, we leave medical science for the realms of astrology. "The fault, dear Brutus, is not in our stars, but in ourselves."

The Virus of Encephalitis Lethargica

There seems little doubt that encephalitis lethargica is due to a filtrable virus. Here we can admit an ætiological resemblance to influenza. From one of von Economo's first cases in 1916–17 von Wiesner inoculated brain matter, taken from a fatal case of encephalitis lethargica, into a monkey, which exhibited lethargic symptoms.

von Wiesner erroneously regarded a symbiotic diplostreptococcus as the causal organism.

McIntosh inoculated material from eight of the fatal cases in the English outbreak of 1918 into *Macacus rhesus* monkeys, with no definite results. Loewe and Strauss (1919, 1920) and others obtained a virus after experimental inoculation of encephalitic material into rabbits, but a spontaneous chronic meningo-encephalitis in rabbits was later described (Oliver 1922, Twort 1922, McCartney 1924). Levaditi's virus (1922), also recovered from rabbits, was found to be identical with the virus of *herpes febrilis*, although work by Perdrau (1925, 1936) and by Da Fano and Perdrau (1927) suggests that the encephalitic virus may bear some relation to the virus of herpes.

In 1919 McIntosh (1920) succeeded in transmitting encephalitis lethargica to a *Patas* monkey with material from one of the fatal cases in the Derby institutional outbreak, which I investigated. A filtered emulsion of cerebral and spinal tissue was used. On examination Turnbull found that the monkey's brain showed lesions similar to those found in human cases of encephalitis lethargica. Subsequently, McIntosh and Turnbull (1920) reported the successful transmission in series of experimental encephalitis lethargica to monkeys and rabbits which completed the evidence necessary to show that the disease is caused by a living virus. Additional proof was provided by the spontaneous infection with encephalitis lethargica of a *Macacus cynomolgus* monkey kept as a control along with an inoculated monkey. McIntosh and Turnbull pointed out that this was the first indisputable occasion upon which experimental transmission of encephalitis lethargica to an animal was successful. This work by McIntosh and Turnbull has not received the recognition it deserves, mainly because other investigators have failed to repeat the experiment. In my view this is because encephalitis lethargica runs a protracted course, as a rule, and the virus is no longer active in the cerebral tissues by the time the patient is dead. This would explain the failure of McIntosh's earlier experiments. But the successful experiment was inoculated with material from a fulminating outbreak of encephalitis lethargica ; twelve women were affected and there were five deaths. The patient from whom the material was obtained died within eight days of the onset of her disease. So virulent was this outbreak that death occurred before the inflammatory reaction characteristic of the disease had time to develop in the patient's cerebral tissues. In another case of mine in the 1918 outbreak, in which death occurred five days after onset, the inflammatory reaction, though present, was slight in degree in the brain. In Lereboullet and Hutinel's case (1919), which proved fatal after a week's illness, the histological findings were almost completely negative, although the clinical symptoms were typical of encephalitis lethargica. von Economo, I find, notes similar instances. He writes :—

> "In hyperacute cases, particularly as seen during the epidemic of 1920, where simultaneously with the hyperkinetic syndrome a grave toxic condition often developed, many cases revealed at the post-mortem examination no other positive finding than an œdema of the brain-substance, cloudy swelling of nerve-cells and an increase of glia nuclei. This shows that there are cases of encephalitis lethargica with a fatal issue before the signs of an inflammatory infiltration of vessels, &c., have had time to develop."

The delicate nature of the virus is indicated also by the fact that it died out eventually after transmission in series by McIntosh and Turnbull. This may prove to be of epidemiological significance in explaining the waning of an epidemic of encephalitis lethargica.

Route of infection.—As with cerebrospinal fever and acute poliomyelitis, it seems a fair assumption that the virus of encephalitis lethargica first affects the upper respiratory passages ; here it may either lurk and give rise to the carrier phase in the person affected, or may pass on to attack the brain. There is no definite catarrhal stage associated with its early manifestations, but sore throat is a frequent concomitant. In view of the frequency of initial conjunctivitis, the virus may possibly reach the brain by the orbital route ; infection by the gastro-intestinal route is also a possibility.

Evidence for Regarding Encephalitis Lethargica as an Epidemic Disease

As I have shown elsewhere (Milroy Lectures, 1925), the epidemiological evidence which is already available in regard to cerebrospinal fever and acute poliomyelitis greatly facilitates an understanding of the behaviour of encephalitis lethargica. In addition to the experimental evidence of transmission of the virus the chief facts relating to the spread of encephalitis lethargica by personal contagion may be thus summarized :—

(1) The restricted topographical distribution of cases. I found this in 1918 in certain districts, notably in the county borough of Stoke-on-Trent. The same tendency for examples of encephalitis lethargica to clump in certain areas of a town or city was noted in 1924 in Sheffield, Bristol, and elsewhere, and is probably associated with density of population and increased opportunities for case-to-case infection. Parsons (1922) found in Bristol and other towns that this topographical distribution tends to be the same in different epidemic years—a circumstance which suggests the presence of endemic foci of the disease.

(2) The examples of multiple cases in families and localized outbreaks in small communities.

Dr. Parsons (1922) and I have put on record in official reports several examples of multiple cases of encephalitis lethargica in families and Netter, Van Boeckel (1920), Kling and Liljenquist (1921), and others have reported a number of similar instances. The institutional outbreak of encephalitis lethargica in a home for girls at Derby in 1919, where 12 persons were attacked out of 22 inmates and there were 5 deaths, has been already mentioned. John and Stockebrand reported a similar outbreak at Mulheim in 1922. Here 28 cases with 13 deaths occurred in twenty days.

(3) Examples of case-to-case infection where infection from a common source was apparently excluded have been reported by R. J. Reece (1919) and others.

(4) The association of mild and ambulant cases with declared cases of encephalitis lethargica. Like cerebrospinal fever and poliomyelitis, encephalitis lethargica has its mild and abortive cases ; through their medium the conveyance of infection from one person to another seems more than probable. In the Derby outbreak I described three abortive cases which affected all the members of the staff of the Home. The symptoms were slight, comprising nausea or vomiting and diarrhœa, "fainting turns", and stiffness in the muscles of the neck. One patient had slight double ptosis which soon cleared. The attacks of illness lasted for one day. A number of similar instances were encountered in 1924 in Liverpool, Sheffield, and elsewhere.

Epidemic hiccup seems to be an example of encephalitis lethargica of a mild type. The disease is infectious ; it has been seen in definite association, for instance, in the same household with encephalitis lethargica, an attack of hiccup may precede or accompany the nervous symptoms of the major disease, and there is good reason, in view of the cumulative evidence, for regarding epidemic hiccup as a mild or frustrated form of encephalitis lethargica.

The epidemiological concept of encephalitis lethargica is, therefore, similar to that of various epidemic diseases of the central nervous system ; thus, while associated groups of cases or definite epidemics sometimes come to light, the ordinary train of evidence is that only here and there does the widespread infecting agent find an individual who reacts with an unmistakable illness manifested by a characteristic syndrome. Alternatively, the agent may infect the individual with such a massive dose, or in such a special manner, that the characteristic disease is produced. In other words, for every definite and characteristic case of encephalitis lethargica there is a large and indeterminate number of people who receive and carry the infection without themselves suffering noticeably, or at all.

Evidence for the Existence of Other Forms of Epidemic Encephalitis

Epidemiology has come to mean the study of disease as a mass phenomenon. Sometimes a dividing line is drawn between the epidemiologist and the clinician. This

hinders progress, for no man can be a successful epidemiologist in the field unless he is also a skilled clinician. The founders of modern epidemiology, for instance William Budd and John Snow, were highly competent medical practitioners. The vital statistician need not necessarily be a graduate in medicine, but he is dependent upon the knowledge of the clinician for the straw with which he makes his mathematical bricks. If Sir William Jenner had not distinguished between typhus and typhoid fever, an epidemiologist working in a country where both diseases prevailed would naturally treat them as one, and his mathematical curves would, I presume, be seriously vitiated. Epidemiology must ever be dependent upon medicine. This principle must closely be remembered in the epidemiological study of encephalitis lethargica.

For Sir Thomas Browne's prophecy has come to pass. With the modern aids to dissemination of knowledge and intercommunication between the four quarters of the globe, Asia, Africa, and America have brought in their list of epidemics of encephalitis, Pandora's Box has swollen and there is, indeed, " a strange pathology ".

I have already referred to the increased number of cases of encephalitis recorded in recent years as sequelæ of the acute infectious diseases and to the appearance of cases of post-vaccinal encephalitis. During the past fifteen years I have seen a number of sporadic cases of polio-encephalitis in addition to the examples occurring in epidemics of poliomyelitis along with the spinal form of the disease. There can be little doubt, as was evident in the Broadstairs and other recent outbreaks, that the virus of poliomyelitis is displaying a greater tendency in some instances to attack the brain rather than the spinal cord. This cerebral type of poliomyelitis has to be distinguished from encephalitis lethargica.

In Japan several outbreaks of encephalitis have occurred during the past hundred years. The disease is known as " summer encephalitis " from its prevalence in the hot summer months. A large outbreak occurred in the summer of 1924, when there were over 7,000 cases with a fatality rate of 60%. Another large epidemic was recorded in August–September 1935 ; it caused about 5,000 deaths. Meningeal phenomena with fever and semiconsciousness predominate. The disease is due to a filtrable virus transmissible to monkeys and rabbits (Takaki 1926, and Taniguchi 1935). It is distinguishable both clinically and pathologically from encephalitis lethargica, and bears a close resemblance to the Australian-X-encephalitis described by Cleland and Campbell. This latter disease occurred in New South Wales in 1917 and 1918, and again in 1922 and 1926. The fatality rate was 70%.

A remarkable outbreak of encephalitis occurred in St. Louis, U.S.A., during the late summer of 1933. Over 1,000 persons were attacked. The case mortality rate, which had an average of 20%, showed a striking increase in relation to the age of the patient : thus under 40 years of age it was less than 10% ; in the 40–50 age-group it was 12% ; in the 50–60 group 21%; in the 60–70 group 38% ; in the 70–80 group 56% ; and in the 80–90 group 80%. In over half the fatal cases death occurred in the first week. Pathologically, the lesions differed in several respects from those of encephalitis lethargica. The disease was transmitted to monkeys and a filtrable virus was recovered, distinguishable by serum tests from encephalitis lethargica and poliomyelitis, and by animal tests from Japanese encephalitis. The careful study of this new clinical entity by American workers is a striking tribute to co-ordinated investigation.

These examples from Asia, Australia, and America indicate that the epidemiologist must not accept every outbreak of epidemic encephalitis as one of encephalitis lethargica. Equally, as von Economo, Redlich, and Sicard pointed out, not every case of encephalomyelitis of unknown origin should be described as encephalitis lethargica.

Encephalitis Lethargica as an Independent Disease

One of the characteristic features of epidemics of encephalitis lethargica is the different types of nervous manifestations which they present, or to use a more sonorous

description, "their symptomatological polymorphism". From the clinical point of view, broadly three types are distinguished: (1) General disturbance of the functions of the central nervous system but without localization; (2) various localizations in the central nervous system; (3) mild or so-called abortive cases. As I observed in my original account of the disease in 1918, the characteristics of one clinical type are often shared by another type, and it is sometimes difficult to say which characteristic predominates. An ataxic case may have severe ophthalmoplegia, while tremors may appear in all types of case. The various types in an epidemic show signs of common identity. The resemblance is not only evinced by the general symptomatology but is shown by the gradual merging of the cases of one type into cases of another type: occasionally, the change from one form to another takes place in an individual patient. In each single epidemic certain types predominate, e.g. in one epidemic the lethargic-ophthalmoplegic type prevails, in another the bulbar-paralytic, amyostatic, or hyperkinetic. These might seem to be different diseases were it not for their simultaneous appearance in one and the same epidemic. Further, as von Economo stated, "the variety within the individual epidemic does not only refer to the neurological aspect of the disease; there are also other differences between one locality and another, one epidemic and another—differences in the general toxicity of the affection, the mortality, the course of the disease, and even the frequency of the dreaded sequelæ."

In spite of this protean aspect of encephalitis lethargica, there is overwhelming evidence from the clinical, pathological, and epidemiological standpoints that encephalitis lethargica is an independent disease, and is distinguishable from the other forms of epidemic encephalitis which are occurring and which are being identified.

One further clinical point may be of interest to the epidemiologist. When encephalitis lethargica first appeared, both in Vienna and in England the predominant type was the somnolent-ophthalmoplegic type, a lesion in or near the 3rd nerve nucleus. Von Economo considered that this type should be regarded as the basic form proper of encephalitis lethargica. My own observations would support this view. In 1926, Dr. G. Ashton and I made a study of the clinical records of 42 insured patients whose deaths were certified as due to encephalitis lethargica in 1924. The largest group (15 cases) consisted of cases with 3rd nerve paralysis. I said then: "The impression is obtained that the incidence of encephalitis lethargica continues to fall largely within this group, but that unless careful and sustained observation is maintained from the beginning of the illness the mesencephalic localization is apt to be overlooked, for it is often slight in degree or transient, and secondary physical signs are regarded as the salient and primary features of the illness."

Through the courtesy of Dr. Isabel Wilson of the Board of Control, my attention has been drawn to a monograph entitled "Epidemic Encephalitis in Saxony", by Dr. Walter Büsse of Gottingen, published in 1933. His figures show a similar predominance of the basic somnolent type of encephalitis lethargica in the 520 cases studied.

Conclusion

Encephalitis lethargica has been notifiable in England and Wales since 1919. The highest year of incidence was 1924, when 5,039 cases were notified, with 1,407 deaths. Since that year the incidence has gradually declined, and from 1930 onwards the deaths as aftermaths of the severe epidemic incidence have exceeded the notifications. In 1936, 269 cases were notified, and there were 686 deaths.

From time to time sporadic cases are notified and, occasionally, multiple cases in one family come to light. For example, in March 1936, four cases in one family were reported from an urban district. The epidemiologist cannot,. therefore, dogmatize upon the future behaviour of this malady. He can only hope that the declining incidence means that it will become rare enough again to disappear from our records.

The various aspects of the disease which we have considered denote that encephalitis lethargica is a clinical entity and is to be distinguished from other forms of epidemic encephalitis which are appearing in our midst. Our clarification of this problem, based at first on clinical and epidemiological work, has been confirmed and strengthened by the remarkable increase within quite recent years of our knowledge of the filtrable viruses. As Topley and Wilson (1936) remark, " Bacteriology is on the march again ", and we may add that epidemiology is once more sharing in its achievements.

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[*October* 8, 1937]

Popliteal Aneurysm.—DUNCAN C. L. FITZWILLIAMS, C.M.G., F.R.C.S.

W. C., an unemployed labourer, aged 53, referred by Dr. Fell of Colchester. Admitted to hospital October 1, 1937.

History.—A painless swelling appeared in the right foot, calf, and lower thigh three weeks ago. This has changed colour in the last nine days and is now dusky.

Examination.—There is a pulsating tumour on the inner side of the lower part of the thigh, which is 19 in. in circumference as against $15\frac{3}{4}$ in. on the sound side. The swelling is 7 in. long. Over it there is an old scar of a pitchfork wound when the patient was 15 years old.

A few days later the swelling was much larger than it is at present, and is gradually decreasing. It is not painful or tender. Pulsation is small but very distinct; the swelling is firm on pressure, not elastic. Dr. Fell suggests that there has been a hæmorrhage which is consolidating. It appears to be a traumatic aneurysm which is now organizing. A "sawing wood" bruit is heard faintly over it, but better over the artery 2 in. below Poupart's ligament.

X-ray examination negative. Wassermann reaction positive. Blood-pressure: Right leg, 120; left leg, 145, level of aneurysm.

Sarcoma.—DUNCAN C. L. FITZWILLIAMS, C.M.G., F.R.C.S.

D. R., male, aged 62, miner. Admitted to hospital September 30, 1937.

History.—The first week in August he had a pain below the right knee, which spread up to the lower part of the thigh in about ten days, so that he could not walk. On examination he found a swelling in the thigh, less than half the size it is now. His face looks pale and anxious, and he has not walked since August, so his muscles are flabby and wasted, but he is not losing weight. There is a swelling approximately 6 in. long on the upper part of the thigh, in front and rather to the outside. $6\frac{1}{2}$ in. below the anterior superior iliac spine, the thigh measures $18\frac{1}{2}$ in. as compared with 16 in. on the opposite side. The swelling seems to be below the rectus and sartorius muscles, but is chiefly in Scarpa's triangle, displacing the vessels inwards. Soft small glands can be felt on both sides below Poupart's ligament.

All movements of the thigh are painful and restricted. The adductor muscles seem to be free and there is nothing in the ham. Nothing is to be felt in the abdomen. X-rays show that the bone is not affected. The swelling is slightly mobile and feels elastic or semi-fluctuant.

Diagnosis: Sarcoma of the soft tissues of the thigh.

Suprasellar Arachnoid Cyst.—KENNETH HERITAGE, F.R.C.S.

Girl, aged 15. Referred to me by Mr. Meadows-Riley and Dr. Ashton.

History (*when first seen one year ago*).—For some years had had difficulty in getting satisfactory glasses. Progressive loss of vision for a year. Had menstruated one year previously, not before or since then. Four months ago onset of severe generalized headaches. These stopped suddenly a month ago. No polydipsia or polyuria. No history of injury, or middle-ear infection.

On examination.—Well-nourished girl, under-developed for her age. No cranial nerve palsies. Gross bilateral papillœdema (five diopters); bi-nasal hemianopia. No other signs in central nervous system. Vision: R., counts fingers; L., hand movements (fig. 1).

X-ray examination.—Slightly "beaten-silver" skull; dorsum sellæ thinned. No calcification. No pineal shift.

A diagnosis of craniopharyngioma was made and a correspondingly poor prognosis

given, as in view of raised intracranial pressure a cyst of the upper anlage was diagnosed.

Operation.—Left frontal osteoplastic craniotomy under avertin and nitrous oxide and oxygen anæsthesia. As the dura was under great tension the left lateral ventricle

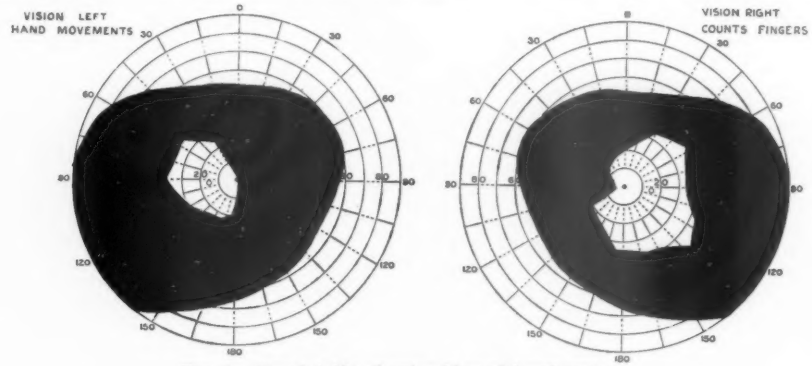


FIG. 1.—Visual fields, showing bi-nasal hemianopia.

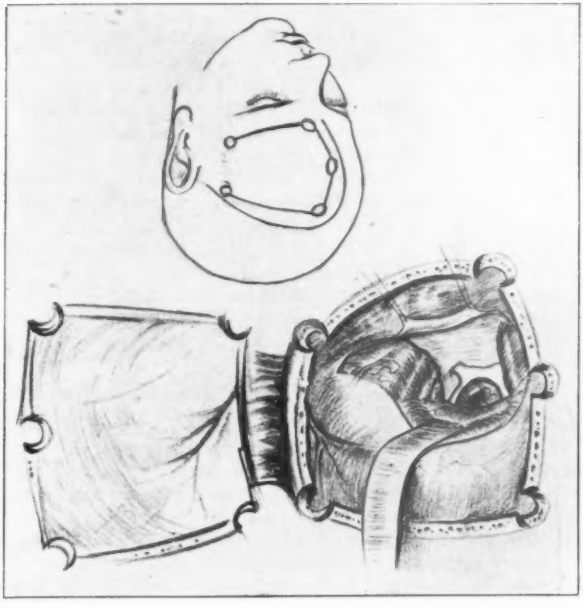


FIG. 2.—Sketch of operative findings, showing retro-chiasmal cyst.

was tapped and *eight ounces* of cerebrospinal fluid were withdrawn. This allowed the left frontal pole to be lifted after incision of the dura. The left optic nerve was identified and traced to the chiasm, behind which lay a translucent thin-walled cyst. On aspirating this, 10 c.c. of a slightly turbid fluid were withdrawn (microscopic

examination showed many crenated endothelial cells only). The superior wall of the cyst was removed, and the dura and skull closed. Slight hypothalamic reaction (pulse 130 ; 100 oz. of urine passed per day) persisted for the first two days.

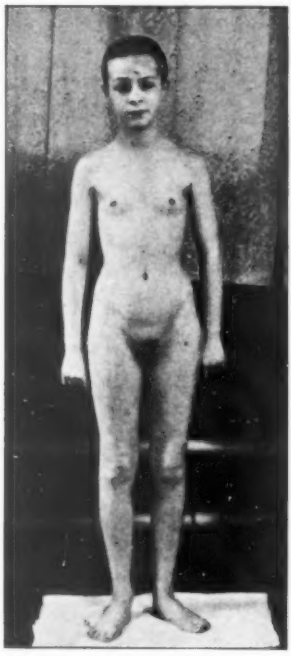


FIG. 3.—Patient ten days after operation.

Papillœdema subsided, and vision improved in the right eye to $\frac{6}{60}$. The nasal half of the right field has increased but no improvement has been noted in the left eye.

The patient is now (one year after operation) free from symptoms and in good health. Normal menstruation has been established.

Diaphyseal Aclasis.—W. G. GILL, F.R.C.S.

Monica C., aged 11 years.

Admitted to hospital complaining of a lump on the right arm, which had appeared at the age of 5 years, and had slowly increased in size. It was not painful, but was causing inconvenience to movement of the shoulder-joint.

On examination.—A normally developed, healthy and intelligent child, with an obvious swelling on the posterior aspect of the upper part of the right humerus. It was bony, hard, and painless, and seemed to rub against the chest wall during external rotation. This bony tumour was excised because of the inconvenience it was causing. The section showed it to be an exostosis consisting of cancellous bone. It had a cartilaginous tip.

Present condition.—The child also presents many other features of diaphyseal aclasis which were noted at the time of admission. Several bony abnormalities can be seen and felt, some more obvious than others. There is a marked cubitus varus on the right side, due to lack of growth at the torn ulnar epiphysis and not to disease of the humerus. Exostoses of tibiæ, fibulæ, and femora, in the region of the knee-joints

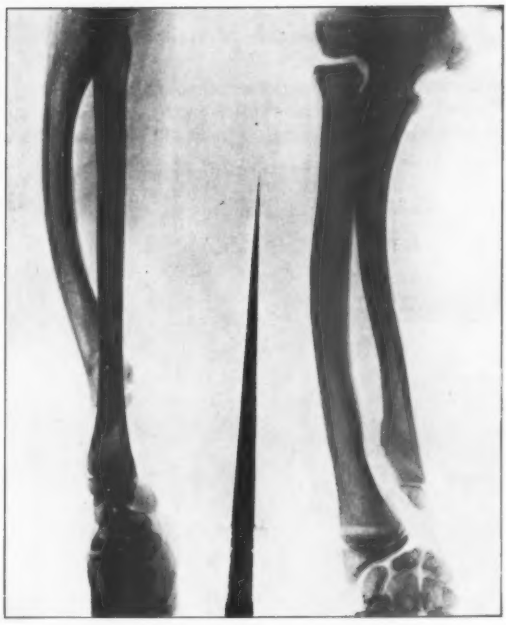


FIG. 1.—Right radius and ulna.

FIG. 2.—Left knee-joint.

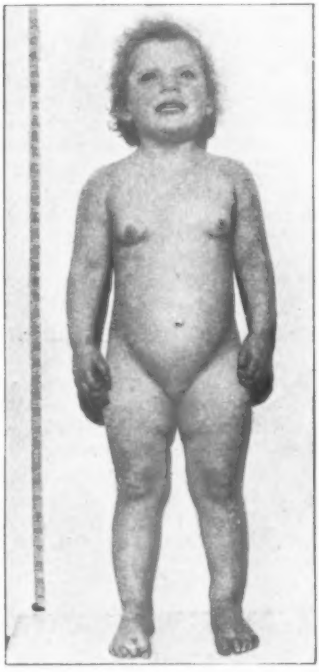
are easily felt. These findings are confirmed by skiagrams (figs. 1 and 2), which also show clearly the widening of the metaphyses, the stippling, and the abnormal trabeculation in the long bones.

There is no family history of the condition.

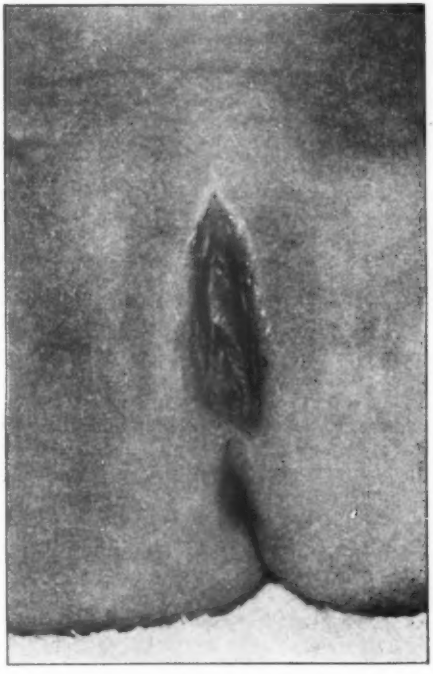
Precocious Puberty in a Female Infant.—R. W. B. ELLIS, M.D.

E. B., a girl, aged 23 months, was well until seven months ago when she began to have vaginal bleeding, occurring at almost regular monthly intervals. The loss of blood is not great, but lasts from two to three days. During the same period there has been gradual enlargement of the breasts.

She was born at term, of normal parents, weighing 11 lb., and was bottle-fed, being given soft solids at 9 months. Chicken-pox at 17 months. There are six other children, all of whom are well ; one other was killed in an accident, and there has been one miscarriage.



Showing breast development and wide hips.



Hypertrophy of labia and sparse growth of hair on pubis.

On examination.—A sturdy, active baby weighing 32 lb. Height 35½ in. Head circumference 19½ in., chest (at nipple level) 21¾ in., abdomen (at umbilicus) 21¾ in., hips 22¼ in. There is well-marked breast-development, the glandular tissue measuring approximately 3½ in. in diameter. The nipples are small and retracted, and surrounded by pale areolae ; no fluid can be expressed. There is a little fine down over the pubis. The hips and thighs are unusually well developed and plump, giving an adult appearance. The labia minora are moderately hypertrophied. On rectal

examination, a firm mass, slightly to the right of the mid-line can be felt in the pelvis.

Radiological examination.—Abdomen: No abnormality seen. Pituitary fossa normal. Wrist: Three centres of ossification present. The long bones appear possibly a little more massive than normal for this age.

Urine: No albumen or sugar; contains less than 25 units prolan per litre (lowest assay attempted). Œstrin content less than 400, and over 40, units per litre—probably well over normal limits at this age. (Dr. W. R. Spurrell.)

Psychological report (Mrs. Norman).—"On the results of the Merrill Palmer tests this child falls within the dull group. However, she refused a number of the tests so that it is possible that she is really rather nearer to the average than the I.Q. indicates. She gave no indication during the interview of any abilities that would rank her above the average child of her age. Merrill Palmer mental age: 19 months. Merrill Palmer I.Q.: 83."

Discussion.—Dr. PARKES WEBER said he thought that cases like this, which were admittedly very rare, should be termed "macrogenitosomia in females, without virilism and with precocious menstruation". A case of this class was recently described in the *British Medical Journal* (1937 (ii), p. 620) and the diagnosis suggested was: "pineal syndrome due to neoplasm or hyperplasia of the pineal gland". But the pineal syndrome occurred almost only in males. He (Dr. Weber) suggested that the macrogenitosomia and precocious menstruation might be due in both cases to a granulosa-cell tumour of the ovary, though this was thought to be extremely rare in children.

Dr. J. D. ROLLESTON emphasized the liability of cases of precocious puberty to precocious maternity and alluded to a case reported by A. Restrepo (*Bol. Clin. Depto. de Antioquia*, June 1937, abstracted in *Paris médical*, October 2, 1937, p. 268) of a girl aged 3 years "who was gradually deflowered by a friend of the house" and gave birth to a normal child at the age of 7 years. Restrepo referred to a paper by Reuben and Manning who had collected 83 cases of pregnancy in girls under 15 years of age, 14 of whom had given birth to stillborn infants.

POSTSCRIPT.—Laparotomy performed by Mr. Nils Eckhof, October 10, 1937. The cervix was considerably enlarged (this presumably being the mass felt per rectum), the uterus less so. Both ovaries were three or four times the normal size for this age, and the lower pole of the left ovary was cystic. This latter portion was removed for microscopical examination. No abnormality of the adrenal glands could be detected.

Histological report (Professor Nicholson).—"Lower pole of right ovary: A follicular cyst with much proliferation of granulosa and a slight luteal reaction, a hæmorrhagic corpus albicans, a scarred corpus fibrosum, ova at various stages of maturation, but no definite tumour."

In 5 c.c. of fluid removed from the cyst no œstrin was detected (Dr. W. R. Spurrell).

Splenomegaly and Meningitis. ? Nature.—J. H. MASON, M.D. (for Dr. THOMAS HUNT).

E. R., aged 28 years; lorry-driver. Admitted to hospital July 29, 1937, complaining of pains in limbs and back of from three to four weeks' duration.

Past history.—Enteric fever, when aged 12. Frequent sore throats.

On examination.—Temperature 100·5° F. Pulse 84. Respirations 20. Pharyngitis. Epitrochlear glands enlarged. Spleen: Moderate enlargement, firm, painless. Erythematous spots on dorsum of feet. Irregular pyrexia with rigors. Widal test negative. Wassermann reaction and Kahn tests negative.

Blood-count: R.B.C. 4,800,000; Hb. 102%; W.B.C. 8,400 (eosinophils 2%). Urine and fæces cultures: No organisms of significance.

13.8.37: Headache, vomiting, diplopia, and weakness of L. sixth nerve;

optic discs blurred on nasal edges. Cerebrospinal fluid turbid. Cells 3,900 per c.mm. (polymorphonuclears 70%), chlorides 700 mgm. Lange: No change.

Blood-count (19.8.37): W.B.C. 16,000.

31.8.37: Cerebrospinal fluid cells 3,600 (polymorphs 60%); chlorides 625 mgm. Cultures sterile. Leucocytes 11,000. Blood-culture sterile.

Complete recovery. Discharged 14.9.37. Spleen and epitrochlear glands still enlarged.

Dr. HAROLD BALME said that the history of the case was definitely suggestive of *Brucella abortus* infection. In a case previously under his care, enlargement of the spleen, spots on the skin and headache of meningeal type were all present, though there was no evidence of actual meningitis. He asked whether the agglutination reaction of the patient's serum had been tested against the *Brucella abortus* group of organisms, and suggested that this should be done.

? Osteochondritis. Case for Diagnosis.—ERNEST FLETCHER, M.B.

J. D., male, aged 14 years, gives a history of pain and swelling in the feet last winter, particularly noticeable in the little toe of the left foot, but the great toes were also affected, though to a less extent. The pain travelled up to the right knee, and he was unable to walk. In July this year the right knee swelled, and there was some pain in the left temporo-mandibular joint.

Past history and family history negative.

On examination.—The boy is spare and is losing weight. Blood-pressure 140/70. General examination negative. Right knee swollen; some limitation of movement and crepitus. Also crepitus in left temporo-mandibular joint and in big toes. Bilateral pes cavus.

Skiagrams: Left temporo-mandibular joint negative. Pelvis: Synostosis of both sacro-iliac joints. Both hips show some infiltration of surrounding bone. Spine normal. Knees show gross atrophic changes. General decalcification of both feet. Absorption of epiphysis of fifth metatarsal. X-ray diagnosis: Probably osteochondritis. Chest normal. All other bones normal.

Investigations.—Blood-count: R.B.C. 4,680,000; Hb. 86%; C.I. 0·92. *Differential:* Polys. 37%; lymphos. 60%; monos. 2%; eosinos. 1%. Wassermann reaction, negative. Blood sedimentation rate varies from 20 to 25 mm. in one hour. Serum calcium, 11·4 mgm. per 100 c.c. Plasma phosphate, 2·25 mgm. per 100 c.c. Blood uric acid, 2 mgm. per 100 c.c.

A Condition Resembling Rheumatic Fever with Arthritis, in a Man aged 48. ? Nature.—ERNEST FLETCHER, M.B.

E. D., a plumber.

Past history.—Herpes zoster fourteen years ago, left thorax. No history of rheumatic fever.

History of present condition.—June 1937: The patient had pain across the toes of the right foot, spreading up to the right knee. The leg swelled from the knee down and was painful, hot and tender, with a high temperature. At the end of August he was admitted to hospital. His temperature was then 100° F. and pulse-rate 96, and he sweated freely. The right knee and both wrists were swollen, hot, and tender. No effusion.

Progress.—He was given 40 gr. of sodium salicylate three-hourly, for eight days. At the end of that time the temperature was normal and the pulse-rate had diminished. Blood-pressure 110/70.

X-ray examination.—Hands show early decalcification throughout. Right knee shows widened joint space. Otherwise all skiagrams normal.

Investigations.—Blood sedimentation rate varies from 48–52 mm. in one hour. Blood uric acid: 1·8 mgm. per 100 c.c. Blood-count (16.8.37): R.B.C. 4,450,000;

Hb. 84%; C.I. 0·94%; W.B.C. 11,500 (which have varied since between 9,000 and 12,000). *Differential:* Polys. 72%; lymphos. 22%; monos 6%. Wassermann reaction, ++. Gonococcal complement fixation test: negative.

Discussion.—Dr. J. D. ROLLESTON said that in view of the tendency for syphilis to simulate rheumatic fever, and of the positive Wassermann reaction in this case, he suggested that a trial should be made of anti-syphilitic treatment.

Dr. PARKES WEBER referred to subacute cases of rheumatic fever in adults, which had sometimes been temporarily supposed to be subacute rheumatoid arthritis. The small joints of the hands tended to be specially involved in these cases, and the reaction to salicylates was slower than in ordinary cases of acute rheumatism in children. Though the heart was less often affected, serious cardiac complications might arise if prolonged rest was not insisted on after the disappearance of the fever.

Chronic Splenomegaly.—GERALD SLOT, M.D., and G. S. CAITHNESS, M.B.

Mrs. H., aged 33.

August 13, 1937: Admitted to Royal Waterloo Hospital complaining of lassitude and exhaustion, with frequency of micturition and "dropped womb".

Examination revealed an enlarged spleen, extending about 9 inches below the costal margin, a generalized moderate enlargement of the lymph-glands, and slight impairment of the percussion note over the lower lobe of the right lung, with prolonged expiration on the same side. She also had partial facial paralysis of left side and gave a history of sudden complete left-sided facial paralysis eight years ago.

Blood pictures and other biochemical investigations made since admission are inconclusive and the condition is still undiagnosed.

Investigations.—Biopsy of enlarged lymph-glands show numerous tuberculous cell systems. Blood-count: R.B.C. 3,820,000; Hb. 75%; C.I. 0·98; W.B.C. 8,200. (*Differential* normal.) Negative indirect and direct van den Bergh reaction. Blood Wassermann reaction negative. Examination of several specimens of sputa was negative for T.B. Skiagram of chest showed increased right-sided basal shadowing.

Dr. PARKES WEBER thought that this belonged to a group of cases in which chronic tuberculosis, notably of the lymphadenoid tissues, clinically somewhat simulated lymphogranulomatosis maligna, and which from the point of view of clinical diagnosis might be shortly termed "tuberculous pseudo-Hodgkin's disease". The spleen in this case, which, owing to prolapse, appeared larger than it really was, might be tuberculous like the superficial lymph-glands, or its enlargement might be due to obstruction in its pedicle. Dr. Weber suggested that the infection in the present patient might have been from milk, of which she had taken a great deal, her husband being connected with the milk trade.

Multiple Bone Tumours in a Boy aged 16 (Ewing's Tumour).—E. STANLEY LEE, M.S.

Patient first admitted to Westminster Hospital 27.8.37.

History.—Two months previously had had fleeting pain in left wrist. Three weeks previous to admission had had rather severe pain in same site after rowing, considered to be a strain. One week before admission again noticed the pain, and at the same time developed pain and swelling of right upper jaw. For three days had had occasional pains in right index finger and right ankle. For three days also right upper teeth had been painful and very tender.

Clinical examination: Healthy appearance. Intelligent. Temperature 99° F. Pulse normal. (1) Swelling of right maxilla, due chiefly to thickening of alveolus. All teeth in this jaw loosened and tender. Swelling obvious both on face and palate (fig. 1). (2) Tender swelling of styloid process of left radius (fig. 2). (3) Swelling of second right metacarpal (fig. 3). No changes in skull or other bones.

A diagnosis of osteomyelitis was made, and eight teeth were extracted. The

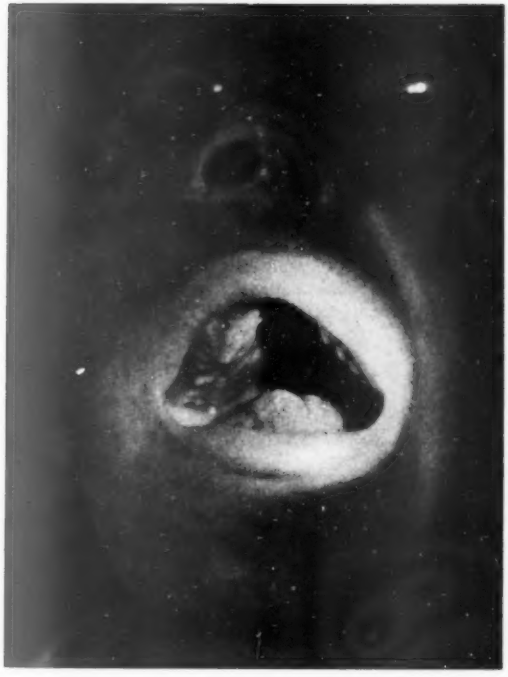


FIG. 1.—Swelling of right face and palate.

FIG. 2.—Lesion involving both shaft and epiphysis at lower end of left radius.

FIG. 3.—Lesion of right second metacarpal.

teeth were not obviously abnormal, and in view of the failure of the swelling to subside, the following investigations were made :

30.8.37 : *X-ray examination.*—Face : Some blurring of alveolus and opacity over right antrum (fig. 4). Left radius : Obscure changes in styloid process, compatible with inflammation. Second right metacarpal showed spindle-shaped periosteal reaction. Blood-count and urine healthy. No Bence-Jones protein. Kahn test negative. Blood calcium, phosphorus, and phosphatase, normal.

Subsequent progress.—On 3.9.37 the right antrum was explored by turning up a flap of the alveolar margin. No pus was found, but some granular and spongy bone was removed. Only *M. catarrhalis* could be grown from this specimen, however, and the histology raised a suspicion of Ewing's sarcoma. On 21.9.37 the size of the

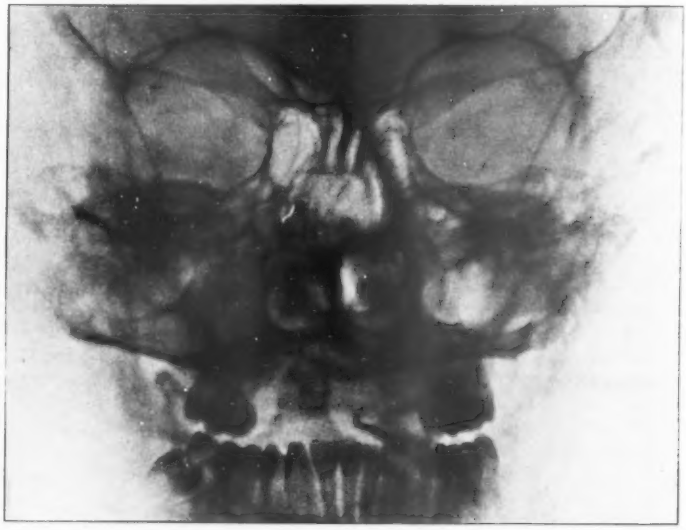


FIG. 4.—Skiagram showing opacity of right antrum.

left radius swelling had greatly increased, and it was decided to explore this to obtain a specimen free from inflammatory changes. A grey firm tumour was revealed, surrounding the brachio-radialis tendon, and cutting with the consistency of an apple. Microscopical examination of a section confirms the diagnosis of Ewing's tumour.

Response to radiation.—Only the left wrist has so far been treated, and after three treatments the tumour has almost disappeared. This rapid response is of course confirmatory of the diagnosis.

Unusual features.—(1) The apparently simultaneous onset of tumours in three bones. (2) The bones affected are most unusual. (3) The radiographic appearances in the left radius are quite atypical in that the metaphysis and epiphysis are alike affected. The disease seems to have begun in the styloid process. (4) Whichever of the lesions is regarded as primary, the sequence is, I think, one not yet reported.

Section of Orthopædics

President—A. Rocyn Jones, F.R.C.S.

[*October 5, 1937*]

The Evolution of Orthopædic Surgery in Great Britain

PRESIDENT'S ADDRESS

By Arthur Rocyn Jones, F.R.C.S.

It is exactly a hundred years since W. J. Little performed the first tenotomy in London, and thereby began a new way of treating deformity, a way that led by slow steps to the emergence in this country of orthopædic surgery as we now know it. Little, at the age of 2 years, fell a victim to infantile paralysis which left him with a fixed talipes equino-varus deformity. Later in life he was a student at the London Hospital, and during this period he sought treatment for his disability, but no one would undertake it. The surgical attack on deformity had already been attempted here and there, but invariably disaster, through suppuration, was a melancholy reward. But in 1834 Little read that Stromeyer at Hanover had obtained some success in the treatment of club-foot by the subcutaneous cutting of tendons with a small narrow-bladed knife introduced through a tiny stab wound of the skin. The following year he was at Hanover submitting his deformed foot to the operation, and the measure of improvement was enough to convince him of the real worth of tenotomy for the cure of deformities. Little learned the technique of the procedure and was allowed to operate himself upon several patients in Germany before he came home.

The Introduction of Subcutaneous Surgery

On February 20, 1837, he performed his first tenotomy in London, and for the next few years he set himself to arouse the interest of the public to the deplorable state of the crippled poor. As a result of his efforts the Orthopædic Infirmary was started in Bloomsbury in 1840, with Lord Chancellor Eldon as its Chairman. The institution at once began to attract much public sympathy and support, so that soon greater accommodation was needed. A larger building was found in Hanover Square to which the work was transferred, and here the hospital reopened its doors with 50 beds. In 1845 a Royal Charter of Incorporation was granted, and the name of the institution was changed to that of the Royal Orthopædic Hospital. Besides working to found the hospital, Little, in 1839, published his classical work "A Treatise on Club-Foot and the Nature of Analogous Distortions including their Treatment both with and without Surgical Operation". This was the first English contribution to orthopædic surgery. The same year he was appointed Assistant Physician to the London Hospital. This post made his position somewhat anomalous. He had been forced into sponsoring the introduction of tenotomy but, as a physician, he had some diffidence in advancing this new remedy further, and it was only on the advice of his senior colleagues that he continued to practise surgery but only to the small extent that is involved in subcutaneous tenotomy. Thus encouraged, he continued the study of crippling disabilities and during the next decade he delivered his "Lectures on the Deformities

of the Human Frame". These subsequently appeared as a book and amongst other matter he described an hitherto unrecognized malady to which Duchenne twelve years later gave the name of " pseudo-hypertrophic paralysis". In 1861 he read before the Obstetrical Society of London his well-known paper on infantile spastic paraplegia, based on an experience of 63 cases. The malady afterwards became known as " Little's disease ". All his writings bear testimony to his greatness as a clinician. But the significance of W. J. Little lies in the fact that it was he who first drew attention to the need for a systematic attack by surgery on the problem of crippling disabilities, and he even went so far as to found a hospital for their study and cure. For a time there were signs of much enthusiasm in relation to the prospect of the prevention and correction of deformity. But experience of subcutaneous surgery gradually revealed its limitations and that in its application a careful choice of the right type of deformity was important. Even after tenotomy frequent manipulation and the wearing of an apparatus were needed to obtain correction. And for the next forty years tenotomy, manipulation, and appliance constituted the tripod of orthopædic treatment ; there was none else. But it must be confessed that operative surgery in general was hardly more exalted, for operations of emergency, such as amputations and abscess drainage, made up the greatest part of the work of the operating surgeon. That fertile field, the abdomen, was untouched, and in the case of a compound fracture the scales were heavily weighted on the side of the loss of life or limb.

The Introduction of Anæsthesia and Antiseptic Surgery

No progress was possible in surgery until an operation became safe and painless. Both these conditions were fulfilled within twenty years of each other, but it is indeed surprising that—although Sir Humphry Davy, the true discoverer of anæsthetics, as early as 1800 produced complete experimental evidence of the power of nitrous oxide to induce safe anæsthesia—it was not until 1846 that Robert Liston at University College Hospital performed the first operation in these islands under an anæsthetic, but using ether. It is something of a tribute to Davy's discovery that over 130 years later nitrous oxide should still be regarded as the safest general anæsthetic and be the most highly favoured. Following on the employment of anæsthesia in surgery came Pasteur's announcement of a germ origin for disease. This teaching revolutionized the whole of medicine, and led in 1864 to the introduction of antiseptics, whereby Joseph Lister made surgery safe. Anæsthesia and antiseptics opened the floodgates to a sea of progress in surgery ; and the tide soon reached the channel of orthopædic surgery. Perhaps William Adams, of the National Orthopædic Hospital, was the first to go forward by shifting the attack on deformity from the soft tissues to the bone structures. In 1871 he performed a subtrochanteric osteotomy for flexion and adduction deformity of the hip, due to ankylosis. He was closely followed by Lister's two pupils, Thomas Annandale of Edinburgh, and William MacEwan of Glasgow. Annandale extended osteotomy to the cure of genu valgum, and the same surgeon in 1879 successfully removed a loose cartilage from the knee-joint, under antiseptic precautions. During the next decade the complete technique of this last operation was evolved by Herbert Allingham and others. And as the surgery of the knee-joint had been worked out in this country, this articular region remained a peculiar British territory for several years. But in the seventies no one played a greater part than MacEwan in establishing osteotomy as a settled surgical procedure. Trained early in the principles of antisepsis, he proceeded to the cure of the rachitic cripples of Glasgow by osteotomy. At this period too he began his experimental researches on bone growth and the function of the periosteum. The knowledge gained with dogs in the laboratory led him on to aid in the regeneration of bone in man. And in 1880 he watched, in a child, the regrowth of a humerus destroyed through osteomyelitis, after he had sewn bone chips in the bed of the bone. This

operation of MacEwan's is of fundamental importance in bone surgery, for it was the first successful deliberately-planned bone graft operation ever performed.

The Principle of Complete Rest in the Treatment of Diseased and Injured Bones and Joints

Working in another field at this time there was a surgeon of an entirely different type. From Liverpool, Hugh Owen Thomas was protesting against the prevailing ideas in the treatment of diseased joints, fractures, and paralytic deformities. He was greatly influenced by the teaching of John Hilton in his lectures on " Rest and Pain " delivered at the Royal College of Surgeons in 1862. In the treatment of inflamed and injured tissues the governing principle for Thomas was the securing of complete rest and to attain this ideal he strove for years, aided by his inventive genius. With his own hands he forged his appliances, improving and discarding models as experience dictated, until at last he evolved the now famous hip and knee splints so amazingly simple in design that they could be made, as he intended they should, by any village smith and saddler. But it is a great error to think of Thomas only as an inventor of splints ; indeed he never ceased to protest against such an estimate of his work. He was an original thinker in surgery and his appliances were the outcome of much probing of the problem of disease and deformity and of the laws governing restoration of function. The patience shown in checking results before proclaiming his principles of treatment were well indicated by the fact that he had tried his methods out on over a thousand patients before he published his first book in 1875 on " Diseases of the Hip, Knee, and Ankle Joints ". In this work the now-famous hip and knee splints were described and illustrated for the first time. And in diseases of joints, fractures, and early paralysis, Thomas maintained that it was all-important to have what he called enforced, uninterrupted, and prolonged rest, and his splints if properly applied, would secure this. In the treatment of infantile paralysis he again insisted on this, but coupled with relaxation of the paralysed muscles ; an example of this principle in practice is his cock-up splint for drop-wrist. There were many other devices which he introduced, such as the wrench, the cuff and collar, damming and percussing for un-united fractures, and his clinical test for the degree of hip flexion in ankylosis. But his wider fame rests largely on his lower-limb splint or bed caliper. In his fracture work Thomas laid great emphasis on the attainment of proper alignment of the fragments. It was the only sure course for a good functional result, and this clinical advice was of first-rate value in the days before X-rays. Alignment having been obtained, rest for the fragments was essential until firm union had taken place. Thomas himself, in fractures of the lower limb, retained this alignment and secured this rest by means of his now world-famous lower-limb splint consisting of the thigh ring and two parallel bars joined below the foot. He had been treating his lower-limb fractures in this way since the early seventies, but it took forty years and a world war to convince the profession of its value in fracture work. If Hugh Owen Thomas had this splint alone to his credit he would have deserved well of humanity, for the number of limbs it saved and the suffering it alleviated during the Great War were beyond reckoning.

The Emergence of the Orthopædic Scientific Society

In the main the teaching of Thomas was confined to the non-operative side of orthopædic surgery, for Listerian principles hardly affected him. But the introduction of antiseptics had a quickening influence on the younger men, and this was shown by a desire of surgeons, interested in orthopædic surgery, to meet and discuss its problems. At the annual meeting of the British Medical Association in Bristol, 1894, an informal meeting was held with the object of founding an orthopædic society, and on November 3 in the same year the British Orthopædic Society was formed, the avowed object of which was the advancement of orthopædic surgery. Forty members were enrolled.

Three meetings a year were held ; the first took place on January 31, 1895, at the Royal Medico-Chirurgical Society's rooms, Hanover Square, London. Amongst the many papers discussed at its meetings one is of particular interest in view of the discussions on club-foot lately held in Belfast. At Liverpool over forty-two years ago Robert Jones opened a discussion on the treatment of intractable talipes equino-varus. He had given up tarsectomy and came down strongly on the side of manual reduction or the use of the Thomas wrench, with the application of the club-foot shoe. To prove the success of the method, he demonstrated before the Society several patients, with photographs. Some of you will remember his saying what were his tests of cure, and you will be reminded of them again by this quotation from his paper of 1895 :—

> " The foot is not cured until the patient can voluntarily place it in the position of valgus, and he should not be allowed to walk until the foot is so far recovered that each step he takes tends to improve the position of the foot ; in other words until the act of walking becomes a beneficial factor in the correction of the deformity. It is impossible to lay too much stress upon the influence of the over-stretched muscles on the convex side of the deformity in the maintenance of the deformity, or its recurrence."

Among other papers there was one by A. H. Tubby on tendon repair, based on animal and histological research, and another by the same surgeon advocated Paci's manipulative reduction for congenital dislocation of the hip. But in spite of its stimulating discussions, the British Orthopædic Society only lasted a few years. Three slender volumes of its transactions were published, and the very last paper contributed was one on tendon transplantation, by Openshaw. The Society, however, had served a useful purpose, for it had brought together even for only a few years, the men who were interested in orthopædic surgery, and the memory of this co-ordinated effort lingered. They were the same men who came together again fourteen years later, to form in more favourable circumstances this Section of the Royal Society of Medicine. But in the very first year that the British Orthopædic Society started its discussions an event of capital importance occurred, and one full of meaning for orthopædic surgery in particular. In December 1895 Röntgen disclosed to an astonished world his discovery of the X-ray. And thus suddenly to surgery was given the means of knowing the pathology of the living bone and joint afflicted by disease or injury. And so the nineteenth century ended, a century with three phenomenal discoveries of far-reaching importance in medicine ; anæsthesia at the beginning, the germ theory of disease and its expression by antisepsis, in the middle decades and X-rays at the close.

Hospital Reconstruction and the Emergence of the Country Hospital

The early years of the new century were much occupied with hospital organization. In 1900 Dame Agnes Hunt began to establish a surgical home at Baschurch and in 1904 she was able to persuade Robert Jones to visit and operate there. Gradually the home developed into an open-air orthopædic hospital, the first of its kind in this country, and to its visiting surgical staff were added former pupils of its chief surgeon. The hospital was transferred to Oswestry in 1921 and was subsequently renamed "The Robert Jones and Agnes Hunt Hospital". It has done a pioneer work in providing a model for other country hospitals both in regard to open-air treatment, the organization of out-patient clinics, and vocational training. In 1908 the Lord Mayor Treloar Cripples' Hospital was founded for the treatment of surgical tuberculosis with Sir Henry Gauvain in charge. This hospital has since widened its field for the treatment of orthopædic maladies in general. And in 1909 the new Royal National Orthopædic Hospital was opened by King Edward VII. Acting on the advice of King Edward VII's Hospital Fund the three metropolitan orthopædic hospitals, the Royal, the National, and the City, amalgamated, and the new hospital

in Great Portland Street with 200 beds was the result. The work of the hospital increased rapidly, and in a few years the question of a country branch was discussed, but the War delayed the project.

The Teaching Hospital and the Orthopædic Department

Whilst these orthopædic hospitals were appearing, the teaching hospitals in their turn were beginning to direct attention towards the formation of orthopædic departments. But ever since 1864 St. Bartholomew's Hospital had had such a department which in turn had been directed by Willett, Walsham, and Howard Marsh; the last had written one of the best manuals on diseases of joints, as well as many papers on injuries of muscles and joints. Orthopædic departments had also been started at Westminster by Tubby, at the London Hospital by Openshaw, and at the Southern Hospital, Liverpool, by Robert Jones. But the hospital status of all these surgeons was that of a general surgeon in charge of an orthopædic department. The first departure occurred in 1906 with the appointment by Charing Cross Hospital of Mr. H. A. T. Fairbank to its staff, with the status of orthopædic surgeon in charge of an orthopædic department and free from responsibility for any surgical work outside the department. This particular appointment was an early recognition by a teaching hospital of the position which orthopædic surgery should occupy in its organization. This decision was followed in 1912 by St. Bartholomew's Hospital when it appointed Mr. R. C. Elmslie as its Orthopædic Surgeon on similar terms. In the same way, also in 1912 W. H. Trethowan was made Orthopædic Surgeon to Guy's Hospital. Therefore these three hospitals between them established the rule of appointing to orthopædic departments, surgeons who restricted their practice to orthopædic surgery alone. Furthermore, these posts involved the systematic teaching of orthopædic surgery. But long before this period sound teaching in this branch of surgery had been available in several textbooks. The best of these was written by Tubby in 1896. With the appearance of the more comprehensive second edition in 1912 the author included diseases of the bones and joints. Up till that time it was not customary to regard these diseases as coming within the scope of orthopædic surgery. But Tubby in the later edition of his book did much to change that conception. In the preface in the first volume he writes:

"In England, contrary to the custom abroad, works written on 'Orthopædic Surgery', although they have dealt with tuberculosis of the spine, have not included tuberculous and many other forms of diseases of the bones and joints elsewhere. And this in spite of the obvious fact that in the practice of orthopædic surgery a surgeon is constantly called upon to deal with such morbid conditions and their results. It has been my attempt to remedy this somewhat illogical state of affairs, and to treat the subject from its actual standpoint, which is the surgery of the entire locomotor apparatus, dealing not only with actual deformities, but also with those morbid processes which involve potential deformity. It is not claimed that the scope of the orthopædic surgeon's work is thereby enlarged, since he undertakes already the treatment of malformations and deformities of the muscular and osseous systems, which demands a full acquaintance with the pathology of such conditions and with the essential therapeutic methods. A considerable portion of the work has therefore been devoted to a description of arthritic and osseous diseases, as indicated by the amplification of the former title into 'Deformities, including Diseases of the Bones and Joints, a Text-Book of Orthopædic Surgery'."

Whilst the conception of the role of orthopædic surgery was widening and its teaching improving in the schools, at the same time its operative technique was advancing. With the rest of surgery it had followed the drift in the nineties from antisepsis to asepsis and the steam sterilization of dressings. Actually in the matter of bone surgery a further refinement was introduced through the "no touch" technique of Sir Arbuthnot Lane, who evolved this method of operating at the time when he began treating fractures by internal fixation with metal plates in 1905.

The Orthopædic Section of the Royal Society of Medicine

In the years immediately preceding the Great War, there were clear signs of an increasing interest and activity in orthopædic surgery, and this interest was further stimulated in 1913 by the holding of the International Congress of Medicine in London during the whole second week of August of that year. Never before in the history of orthopædic surgery in England did so many leading orthopædic surgeons from the countries of Europe and America assemble together as they did to the Sub-section of Orthopædics over which Robert Jones presided. It was a most impressive gathering. The papers and discussions were fairly representative of the whole range of orthopædic surgery; an idea of some of these may be gathered from the following: The discussion on club-foot was introduced by Lucas-Championière and Whitman; on scoliosis, by Lovett and Schanz; on spastic paraplegia, by Kuttner, Muirhead Little, and Vulpius; on the treatment of ankylosis, by Baer and Putti; on the treatment of tuberculous joints in children, by Dollinger and Ridlon, and on the value of fresh air and sunshine in the treatment of tuberculous joints, by Rollier. But a contribution that attracted considerable notice on account of its boldness and originality was an independent paper by F. H. Albee of New York entitled "Original uses of the Bone Graft as a treatment for Ununited Fracture, Certain Deformities, and Pott's Disease". Albee had already published a preliminary paper two years previously, and this was a further report based on 175 cases in which the bone-graft had been used. And at the Royal National Orthopædic Hospital he demonstrated before the Sub-section the technique of the operation of bone-grafting. Using his motor-driven twin-saw for the purpose, he implanted an autogenous tibial graft into the split spinous processes of the diseased vertebræ of a patient suffering from Pott's disease. The new bone-grafting technique was a great advance in bone surgery and was destined to have wide application by providing a natural fixation for a diseased joint and an incorporating bridge for a gap left in bone by disease or injury. MacEwan in 1880 had paved the way for this new surgery and Albee acknowledged his debt to him. This Sub-section of the International Congress undoubtedly stimulated enthusiasm and further activity in orthopædic surgery in this country. But just before the Congress came to London steps had already been taken at the Royal Society of Medicine to form an Orthopædic Sub-section of the Section of Surgery. And on May 8, 1913 the Council of the Section of Surgery resolved that a Sub-section of Orthopædics be formed. On July 8 the Council of the Sub-section of Orthopædics met for the first time, with Muirhead Little, who bore a great name in orthopædic surgery and who was himself much honoured, as President, and with Mr. Blundell Bankart Mr. Rock Carling as the Honorary Secretaries. And of the Council, Muirhead Little, Robert Jones, Tubby, Openshaw, and Jackson Clarke had all been members of the old British Orthopædic Society and to that extent they were a connecting link with that body. The first clinical meeting was held on November 4, 1913, and was opened with an address by the President. The succeeding meetings were sufficiently successful to encourage the Council of the Sub-section to petition the Section of Surgery to agree to the Sub-section of Orthopædics becoming a full Section. The appeal failed. During the Great War the clinical meetings were suspended, but they were resumed again on October 7, 1919. The members had gathered a rich experience during the hostilities, and the cases and discussions strongly reflected the war period. The meetings were well attended and the success of the Sub-section was well assured. The members therefore again decided to petition for the formation of a full Section. On December 13, 1921, the Council of the Sub-section of Orthopædics met to discuss the procedure of petition, and the following definition of orthopædic surgery was agreed upon: "The surgery of congenital and acquired deformities of the extremities and spine." It was an astute Council that drew up that definition—and that in the post-War period. It was admirable in its brevity and caution and in its traditional stress on deformity. But contrast this definition with that of Tubby's, in a textbook

even of 1912, which reads "The surgery of the entire locomotor apparatus dealing not only with actual deformities but also with those morbid processes which involve potential deformity." The petition proved acceptable to the Section of Surgery, and the Council of the Society therefore resolved to constitute a Section of Orthopædics. The new Section held its first meeting on February 7, 1922. Ever since its formation it has provided a ready forum for the consideration of difficult clinical cases or of those of unusual interest. And during each session at least two meetings have been devoted to a full dress discussion of some orthopædic problem and on occasion a distinguished foreign surgeon has been invited to address the Section on special work for which he is well known; amongst such distinguished visitors have been Albee, Scudder, and Smith-Petersen. But although the Sub-section of Orthopædics was started in 1913 the Section itself owes much of its vitality to influences which began during the later stages of the War.

The War Period

When the great catastrophe of 1914 occurred, a deluge of limb casualties followed. After hurried improvisation by the Army Medical Service to meet this bewildering situation it became abundantly clear to those who had vision to penetrate the problem, that such a devastating time in human affairs demanded a special organization, unknown to peace, to deal with it. One of the first to grasp this was Robert Jones. He not only had the foresight but he was equipped at all points for the emergency. Trained from his boyhood by Hugh Owen Thomas in orthopædic principles, he passed on to the surgical staff of the Southern Hospital at Liverpool, and became a skilful general surgeon. But his succession to Thomas, and his natural bias, kept him at orthopædic surgery, and from the early nineties onwards he took a leading part in everything connected with it and wrote extensively about it. And almost on the eve of hostilities it was he who was chosen to preside at the world gathering of orthopædic surgeons at the International Congress of Medicine. Of his extraordinary personal qualities it is difficult to speak with restraint, and therefore it is best to be content with mentioning three only: his modesty, his capacity for warm friendship, and his skill as a persuasive negotiator. Such briefly were the signs pointing to the fitness of the man for the nation's emergency. Starting off as a Captain of the 1st Western General Hospital he was soon promoted Major, and toured the hospitals in the Western Command. Thus he wrote of his first impression: "No provision of any sort was made for cases crippled and deformed, and early evacuation was both the instruction and the routine. The result was that many men were discharged from the Army in a very large number of cases totally unfitted either for military or civilian life". To stop this state of things he succeeded in persuading the War Office in 1915 to reserve 400 beds at the Military Hospital at Alder Hey, to which wounded soldiers requiring orthopædic treatment might be transferred from other hospitals. The same year he went to France and gave demonstrations at the casualty clearing stations in the use of the Thomas splints, and these splints became a permanent part of war equipment. The caliper, in particular, saved thousands of limbs and helped in the comfortable transport of the wounded. He also wrote two handy manuals which had a widespread influence on all fronts, the one "Injuries of Joints", and the other "Notes on Military Orthopædics".

In 1916 the Hammersmith Infirmary at Shepherd's Bush was converted into a military orthopædic hospital on the lines of Alder Hey, and was staffed by young surgeons who were receptive of new ideas. This hospital also served as a training school for orthopædic surgeons; one of the difficulties encountered in the early days of the military orthopædic hospitals was their staffing, for there were not many trained orthopædic surgeons available. The position improved later by the arrival from America of relays of orthopædic surgeons in charge of Dr. Goldthwait, and they were posted to the hospitals. Following the examples of Alder Hey and Shepherd's

Bush Hospitals, other military orthopædic hospitals appeared in different parts of the country, until a complete organization for the orthopædic treatment of the wounded soldier was provided. This was a great achievement and was only accomplished after much opposition and obstruction. It was a great triumph for the persistence and energy of Robert Jones, who in the meantime had been promoted Major-General and Inspector of Military Orthopædics. In 1919 the hospitals passed from the care of the War Office and came under the control of the Ministry of Pensions, and in 1925 Shepherd's Bush Hospital reverted to the Borough of Hammersmith to become later the British Post-Graduate Medical School.

The Post-War Advance of Orthopædic Surgery and the Formation of the British Orthopædic Association

The War had worked a profound change in the status of orthopædic surgery. Before 1914 it was a somewhat exclusive branch of surgery, for outside its own immediate household its principles were but vaguely understood, if at all. But to-day orthopædic surgery is recognized as a very important part of surgery, and even the lay public are quite alive to its capacity to help them.

Furthermore, the War ended with a far greater number of men trained to orthopædic surgery than at the commencement of hostilities, and these men retained their keen interest in bone and joint surgery. To foster this interest in orthopædic surgery was the business of the scientific society, and some turned towards the Sub-section of Orthopædics held in this House. But to meet the wants of surgeons scattered widely a travelling society was needed. Therefore in 1918 Robert Jones and Dr. Robert Osgood discussed the possibility of forming a British Society on the lines of the American Orthopædic Association. The times were favourable and the project was then discussed with Muirhead Little and Openshaw, both of whom supported the proposal. The three British surgeons then sent out a joint invitation to other prominent orthopædic surgeons to come and dine at the Café Royal and discuss the proposed formation of an Orthopædic Association. About fifteen surgeons met together and it was decided to form the British Orthopædic Association. Muirhead Little was elected the first President, with Mr. Harry Platt as Honorary Secretary. The first meeting was held at Roehampton House on February 2, 1918. In 1920 Robert Jones became President and held this office for five years, when he declined re-election, and thereupon was elected Emeritus President in recognition of his exceptional services to orthopædic surgery. The Association has been most successful since its inauguration, and its spring and autumn meetings, whether held in this country or abroad, have always been well supported. It provides a varied and interesting programme, made up of long discussions, short papers, operations, and demonstrations of clinic patients. On any orthopædic procedure under discussion it can be relied upon to provide the best current opinion. And to encourage the advancement of orthopædic surgery the Association offers the Robert Jones medal and prize for a worthy essay. Since the War another Orthopædic Section has been formed, and that in connexion with the Annual Meeting of the British Medical Association. The first independent Orthopædic Section was held at Portsmouth in 1923 with Openshaw as President. The long discussion and short paper is the rule of this Section, and there may be a visit to the local orthopædic hospital if there be one. The discussions tend to follow a more topical line than in the other societies and this presumably in an attempt to interest general practitioner and specialist alike. The Association has rendered valuable service in connexion with scientific investigations, notably by the appointment of a Fracture Committee in 1912 and another in 1933. The report issued in 1935 has attracted a good deal of attention throughout the country and has done much to stimulate hospitals to form fracture clinics.

[*For the verification of certain details in various parts of the narrative my grateful thanks are due to Mr. Bristow, Mr. Elmslie, Mr. Fairbank, and Dr. Charles Hill.*]

Section of the History of Medicine

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[*October* 6, 1937]

Neohippocratism

PRESIDENT'S ADDRESS

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GUIDING principles are necessary for medical practice in the same manner as for life in general. Each of us has his own philosophy of life which guides daily activities, and each of us physicians has a philosophy of medicine, a doctrine or general medical theory, that guides his daily practice. Just as life without guiding principles becomes a vegetative and unimportant existence, so medical practice without a doctrine becomes a blind and ineffective craft, lacking in style.

Medical doctrine or general medical theory represents a synthesis of medical knowledge, but the body of that knowledge is, and always has been, growing and altering. It is the object of those who study medicine from the cultural point of view to unravel the doctrine embodied in the work and practice of the great masters of medicine, and to present it in intelligible form. It is my object to study the doctrine that permeates the work and practice of certain contemporary physicians, and specifically the doctrine known as *Neohippocratism* or *Constitutional Medicine*.

Many of us have an uneasy reaction to the words doctrine, theory, and philosophy. Many pride themselves on being unattached to any general conception of disease or treatment. Like Flaubert's hero Monsieur Homais, we claim to demand "facts", not "theories", though we are liable to find that, like Monsieur Jourdain, who spoke prose all his life without knowing it, we have all the time been unconsciously permeated by a doctrine. The freedom of those who scorn doctrine is the freedom of the weathercock that, in fact, moves with the wind. Even the so-called "ultra-positivist physicians", empiricists old and new, have a doctrine, just as the philosophical sceptics have, for the rejection of general conceptions is itself a doctrine, albeit a sterile one.

Much of our reluctance to own the existence of fundamental principles is due to the inadequacy or misinterpretation of words. We recoil from the phrase "philosophy of medicine" because we tend to identify philosophy with metaphysical speculation. We forget that in the Greek sense of the word philosophy is the synthesis of knowledge that is the ultimate truth in science, and that among the Greeks to combine the qualities of a physician with those of a philosopher was to raise man to the level of the gods. We recoil from the word "doctrine" because it has come to signify assertion, often unwarranted by facts, though the word is a derivative of *doctus*, and implies ultimate scientific truth. We reject the word "theory" because we take it (in the sense of the detective stories) as a guiding hypothesis, whereas, as Sir Clifford Allbutt has pointed out, theory in its original Greek conception is the intuition of the whole truth. We have lowered the significance of these terms as the Greeks lowered the great god Dionysos who was once a vision of the mysterious and the eternal and became a mere god of wine and pleasure.

Yet despite all criticism and contempt, medical doctrine, general medical theory, philosophy of medicine still exists. Even when the ultrapositivist school was at the height of its influence in Paris, Bouchard could insist that no practice is possible without doctrine. Doctrine represents the ultimate synthesis of medical science. And, according to Plato, there is only one science, the science of the general.

Neohippocratism: the Contemporary Doctrine

The doctrine permeating the work of many thinking contemporary physicians goes by the names of Neohippocratism, constitutional medicine, or individual medicine (R. Hutchison). The term "individual medicine" is inadequate because even the organicism and bacterial causalism—the doctrine that preceded Neohippocratism—admitted individual considerations. We therefore prefer the term Neohippocratism or Constitutional Medicine.

The word *Neohippocratism* indicates that our contemporary doctrine is an adaptation to modern scientific research of the doctrine of Hippocrates. Constitutional Medicine indicates that in our contemporary outlook everything centres on the constitution of the patient, the *physis* of Hippocrates, the condition of balance of the integrative system of the body, or the psycho-neuro-endocrine system, as some would now say. The two recent international congresses dealing with doctrine were held at Paris and Salsomaggiore respectively. One was "The International Congress of Neohippocratic Medicine", and the other "The International Congress of Constitutional Medicine".

Neohippocratism, as Castiglioni has shown in his *Storia della Medicina*, succeeded organicism and bacterial causalism, the doctrine in vogue up to the Great War. According to this doctrine a disease was more local than general and frequently due to one "cause", a micro-organism. Treatment was directed to local manifestations and there was a tendency to standardize treatment according to "diseases". This doctrine gave rise to the brilliant results of local exploration, of bacteriology, and of surgery.

According to the Neohippocratic doctrine, disease is general and only in the last resort local. Disease is considered as an expression of the fight of the body, or better the body-mind, against external noxious agents. All the external conditions that have resulted in disturbed health are reviewed, and an attempt is made to help the constitution, the body-mind, to combat the disease. Thus it is the patient, not the disease, that is the centre of consideration. Treatment becomes biological, individual. Standardization disappears.

The following are the principles on which Neohippocratism is based. They are found in the doctrine of Hippocrates and, thanks to the scientific demonstration which I will examine, have culminated in construction of our modern medical doctrine.

The Nominalistic Conception of Nosographical Entities or "Diseases"

This is the first basic principle of Neohippocratism. It was stressed in the critical work of F. G. Crookshank, Richard Koch, and Knud Faber.

According to the nominalistic principle, diseases, such as those described in the current textbooks of medicine, are mere names, artificial categories of classification of the morbid phenomena. They do not correspond to reality, though they help us to understand the condition of the individual patient, by enabling us to arrange our knowledge of morbid phenomena and, through a preliminary labelling of the patient, by providing a frame for our individual diagnostic considerations.

The nominalistic principle is opposed to the realistic—both these terms I use in the sense of mediæval philosophy—according to which diseases have a substantial reality. According to the realists, therefore, diseases are separate things. No serious physician, however, has ever been a realist in this sense, and most medical realists are in fact rather "conceptualists". Conceptualism was the doctrine of Abelard, postulating that universals, and in our medical application, diseases, are concepts existing in our minds and express real similarity in things themselves.

The nominalistic principle, as applied to medicine, can only be understood historically. The first Greek physicians, those of Croton and Sicily in the sixth century B.C., based their practice purely on study of the diseased individual. It was soon found that diseased individuals show an enormous variety of morbid phenomena, and that for purposes of study, some arrangement of observed things was needed. Thus the Cnidian physicians of the fifth century B.C. introduced nosographical

classification. They found that many morbid phenomena occurred with a certain regularity of combination. They abstracted these combinations of symptoms from the individual, and constructed fictional species which they called " diseases ". Such " diseases " were classified on purely clinical symptomatological lines. In this first phase the morbid categories known as " diseases " were symptom-complexes. On this basis diseases were isolated and described from the time of the Cnidians until the beginning of the nineteenth century. The greatest nosographer of modern times working on these lines was Sydenham.

In the earlier nineteenth century the construction of fictional morbid categories, " diseases ", entered upon a new phase with the expositions of the French, British, and Viennese anatomo-clinical schools, and with the German physiological school. Purely symptomatological-clinical standards were abandoned, and more precise criteria, those of the lesions or functional disturbances of the organs, took their place. " Diseases " ceased to represent a series of symptoms and signs occurring with a certain regularity of combination, and were now considered as constituted by a series of symptoms and signs corresponding to a special lesion or a disturbance in the function of an organ. Thus, with the anatomical and physiological schools, " diseases " ceased to be symptom-complexes and became anatomo-clinical or functional syndromes.

During the third quarter of the nineteenth century the conceptions of " diseases " were again modified by the advent of the bacteriological school, which introduced the ætiological—principally the bacteriological—criterion. It no longer sufficed for the identification of a " disease " to take as basis the clinical symptomatology, or the anatomical lesion, or the disturbed functions of an organ. It was necessary to find a special cause—usually a special microbe—for these lesions, disturbances, and clinical manifestations. It was the ætiology more than the clinical manifestations, the functional disturbances or the anatomical lesion, that became the basis of classification of diseases.

Although " disease-morbid category ", as we consider it to-day, is more complete than in the days of the Cnidians and of Sydenham, and more complete even than in the days of Laennec, of Bright, and of Wünderlich—it always remains a fiction, because an abstraction. On the one hand, the ætiological element, the " cause ", is fictional, because it treats only one factor which is arbitrarily taken as " cause ", whereas a single " cause " for anything is meaningless and devoid of reality. Every morbid condition, is, in fact, the result of a combination of many factors. On the other hand, the clinical manifestations, anatomical lesions, and functional disturbances do not correspond to the whole chain of morbid events, but represent only a part of the real " diseased individual ".

In the first flush of the return to Hippocratism all classification and description of diseases was rejected by certain Neohippocratists. They forgot that notwithstanding what we read in many academic discourses in which, contrary to historical truth, Cos and Cnidos are represented as opposed, Hippocrates himself accepted nosographical classifications. Ottomar Rosenbach and more recently Crookshank were among those who rejected all such classifications.

This attitude was, however, soon abandoned. Most Neohippocratic clinicians maintain the importance of nosographical classifications. They know that a disease is only an artificial unity, but they know also that, as Knud Faber expresses it, " To the clinician it is essential. He cannot live, speak, or act without the concept of morbid categories ". We need the concept of " diseases " not only for learning and for classifying our knowledge, but also for diagnosis. The first step in Neohippocratic diagnosis is disease diagnosis. This is the safety-first diagnosis not only because it gives us the predominant ætiological factor and the lesion, but also because it provides, by the labelling of the patient, an adequate frame for individual diagnostic considerations. Peter said that there are no diseases but only patients. This is true, but

without diseases we cannot understand patients. Ottomar Rosenbach wrote "We wish not to classify but to cure". This also is true, but those who have not classified cannot learn clearly, cannot diagnose with precision, and thus cannot cure.

The Principle of the Unity of the Organism

Demonstration of this principle is the next step for Neohippocratism. The principle may be thus formulated :—

The organism is a whole and is the real biological unit. All organs, cells, or organic structures are interdependent and have no real existence save as components of a corporate whole. No organ, no tissue, no organic structure is independent of the activity of the others, but the life of each of these elements is merged into the life of the whole. The unit of human life cannot be the organ, the tissue, the structure, but the whole organism, the whole man. We have to think in terms of organisms ; to use Rhumbler's term, to be "organismists".

This principle was formulated by Sherrington in 1922 in his presidential address to the British Association :—

"The living creature is fundamentally a unity. In trying to make the how of animal existence intelligible to our imperfect knowledge we have for purposes of study to separate its whole into part aspects or part mechanisms but that separation is artificial. It is as a whole or single entity that the animal or for that matter the plant is finally and essentially to be envisaged."

The organismal point of view is opposed to the separatist which dominated medicine in the nineteenth century. The anatomo-pathologists and the early physiologists treated the human being as a bundle of organs more or less connected with each other. Virchow, who gave the ultimate expression to the separatist idea, taught that the body was a colony of cells. The cellular theory was, in effect, that the biological unit was the cell.

Recent work, especially in this country, has demonstrated the inadequacy of separatist principles, and has thus prepared the ground for the Neohippocratic medical doctrine. Britain never submitted to the dictature of Virchow, and biological thought here has always tended towards unity. In an address to the British Association in 1879 George Mivart said, "As the living creature is a highly complex unity, both a unity of body and also a unity of force, a synthesis of activity . . . we need a physiology specially directed to the physiology of the living body considered as one whole".

J. S. Haldane developed the organismal conception with great accuracy and industry. Influenced by the philosophy of Hegel, he taught that biology must deal with whole organisms and not with organs or cells. The biologist has to deal with life, and he cannot understand life without the fundamental conception that "each detail of organic structure, composition and activity is a manifestation or expression of the life of the organism regarded as a separate and persistent whole".

The same principle has also been stressed, though on slightly different lines, by a group of British and American biologists who took as basis the study of structure and development. Among them special mention must be made of E. S. Russell, who summarized his work in his *The Interpretation of Development and Heredity* (1930). This author, giving biological illustration of the Hegelian conception of the whole as prior to its parts, shows that the unity of the organism is primary, and division into cells and organs secondary. The whole determines the parts and not the parts the whole. He upholds C. R. Collingwood's conception, that "the parts are the way in which the whole organizes itself. The cells are subordinate to the organism which produces them and makes them large or small, of a slow or rapid rate of division, causes them to divide now in this direction now in that". With C. O. Whitman he reminds us that comparative embryology shows at every turn that the organism dominates cell formation, using for the same purpose one, several, or many cells,

massing its material, and directing its movement. Similar ideas were developed and demonstrated in the great work of the American W. E. Ritter, *The Unity of the Organism, or the Organismal Conception of Life* (1919).

Works demonstrating even more distinctly the organismal principle are those which discuss the experimental evidence for the integration of the organism, of the body-mind. Oliver and Schafer, as well as Bayliss and Starling, show the role of chemical integration due to the endocrines. They have resuscitated the humoral theories of Hippocrates and the conceptions of the eighteenth-century Hippocratist, Théophile de Bordeu, who is rightly regarded as the pioneer of endocrinology. To these conceptions they have given the stamp of scientific accuracy. Gaskell, Langley, and their pupils, in their work on the vegetative nervous system, have shown its integrating action. Through this system the organs and tissues are correlated in such a manner that the body can act as a whole. Sherrington crowns the work on integration by demonstrating experimentally that the apex of the integrative scale is the cerebral cortex.

British physiologists and physicians are continuing the work on integration, which is recently developed in Sir Humphry Rolleston's *Endocrines in Health and Disease* and in the clinical research of Sir Walter Langdon-Brown on the integration of the endocrine system. These last works set forth the integration of the body as a whole by a system composed of the psycho-associational cortex, vegetative nervous system, and endocrines, all of these being intimately connected with each other under the domination of the brain. It is a return to the old conceptions of Alkmaion, the body-mind considered as an equilibrium of forces under the domination of the brain, as a " monarchy ", the very word used for integration 2,500 years ago.

The Holistic Conception of Disease

According to this principle disease is of the whole organism, of the whole body-mind. It may have local manifestations in cells and organs, but it is never strictly local. Even when local manifestations predominate they do not constitute a local disease but are manifestations of a preceding general disturbance of the body-mind. The holistic principle is in opposition to the localistic principle which was formulated by Virchow in his address to the International Congress of Rome in 1902 in his aphorism " Disease is never general, it is always local of tissues or organs ".

Although the holistic nature of disease could be shown by consideration of the fact that as the organism is a whole disease can be only of the whole, demonstration has followed different lines, clinical and experimental.

Even in the days of strict localistic principles clinicians were trying to arrive at a wider conception. Sir William Gull said in a lecture to students that to give an idea of Bright's disease he should have shown them not the kidneys and heart of the patient in a bottle but the whole patient. Marchal de Calvi, professor at the Val de Grace in 1845, promulgated the "holopathic" theory of disease on the basis of his clinical observations and his study of the ancients. The same conception of the general nature of disease was defended in Paris by Chauffard, who was imbued with the Hippocratic ideas of his alma mater, Montpellier.

A more precise demonstration of the holistic nature of disease, however, was offered by the first medical biochemists, who showed that before the appearance of a lesion in an organ the whole chemistry of the body underwent change—a modification of metabolism, as we should say to-day. The greatest pioneer on this subject was my teacher Albert Robin. Even in the early seventies, in the midst of the intensely localistic conceptions of the Paris school, he demonstrated the existence of chemical modifications in the body, disturbances in the *échanges*, as he said, prior to and conditioning local lesions. As he was a skilled biochemist, a pupil of Guy Lussac, as well as a clinician, he could pursue technical investigations on that line, and in many diseases succeeded in demonstrating a general metabolic phase. The work of

Robin looms large in development of this phase of the history of disease. At the time, however, he was alone in his views and, as often happens to such, he was misunderstood, and his life degenerated into a struggle with his colleagues of the Faculty at Paris.

Demonstration of the holistic nature of disease was made on different lines by those who discovered that preceding the local lesion, and even independent of the local lesion, disturbances of the vegetative nervous system exist. Ricker, the anatomopathologist of Marburg, made important research on the subject, which he summarized in his work, *Pathologie als Natur-Wissenschaft. Relationspathologie für Pathologen, Physiologen, Mediziner und Biologen.* Sir James Mackenzie by his clinical work did much to promote acceptance of the holistic nature of disease on the same lines of vegetative nervous dysfunction.

The holistic nature of disease has been shown also by the finding of psychical disturbances, disturbances of the psycho-associational cortex, preceding and dominating local organic affections. To Charcot principally is due the conception of " psychogenesis ", of local organic manifestations, a theory developed by Freud and by many brilliant physicians who have delved into the mental factor in disease.

Thus the contemporary conception, which is not pure speculation but has been demonstrated by precise experimental and clinical work, is that preceding all local manifestations there are disturbances of psycho-neuro-endocrine equilibrium, which ultimately result in modification of the body chemistry, a disturbance of the humours if we wish to preserve the Hippocratic terminology. This could easily be deduced from what we know of biology. Through the psycho-neuro-endocrine system the organism adapts itself to its environment. Disease is a struggle of adaptation to a changed environment, and thus the first manifestation must be psycho-neuro-endocrine, that is, general constitutional, metabolic, or " humoral ".

The Dynamic Conception of Disease

Disease represents the struggle of the organism against external evils, the attempts at adaptation on the part of the organism to changes in external conditions. By virtue of the inherent characteristics of life the organism tends to remove all factors that threaten life, it tends to cure itself. This conception therefore depends on the general vitalistic principle according to which every living being is animated by a purposive striving to live, to develop and to immortalize itself by procreation, and for the attainment of its ends is " as if " directed by an inner force—the *physis* of Hippocrates, the *vital force* of the Montpellier physicians—through which it overcomes all obstacles to its development.

To the dynamic conception of disease is opposed the mechanistic, according to which disease results simply from external forces which act on the living being as they would act on inorganic material. This conception of disease depends also on the general mechanistic conception of life according to which life is simply the result of external forces, of various stimuli, as John Brown puts it.

The dynamic conception of disease is the essential point of the Hippocratic doctrine. After Hippocrates it was developed principally by Sydenham. It has been maintained by a series of great physicians such as Paracelsus, Van Helmont, Willis, Bordeu, Barthez, Cullen. The mechanistic conception of disease was developed by Asklepiades and his pupils the Methodists. In modern times it has been advocated by Broussais, Rasori, Henle. It dominated the medicine of the early nineteenth century. It sounded more scientific in the days when physics and chemistry were ruled by rough mechanical conceptions. The greatest blow to this conception was the adaptation by physics of a more deterministic and teleological outlook.

At all events in medicine a series of works showed the inadequacy of the mechanistic conception of disease and established the dynamic conception as a precise scientific basis. Clinicians like Albert Robin and Sir James Mackenzie demonstrated that in sickness the patient is really fighting his disease. Anatomo-clinical workers

such as Sir Andrew Corrigan showed the compensatory work of organs to overcome their deficiency. Aschoff in a series of brilliant researches showed the purposive nature of inflammation. Last but not least, the work of Metchnikoff and other immunologists demonstrated scientifically this *vis medicatrix naturæ*.

The Principle of the Ætiological Constellation and the Role of Constitution or Diathesis in Disease

Disease results from the interplay of various external factors to which our organism reacts. We thus must consider ætiologically in any disease a series of external ætiological conditions, comprising modifications of environment and a series of constitutional factors comprising factors of resistance. Every patient, therefore, offers for review a constellation of ætiological factors differing in grouping from that of every other patient.

This principle of ætiological constellation (a term introduced by Tendeloo) or conditionalism (a term introduced by Verworn) is opposed to the principle of causalism, mainly bacterial in nature, that dominated medicine even a few years ago.

The inadequacy of the causalistic conception has been demonstrated even in respect of the external factors. In epidemic diseases the micro-organism is not everything, as has often been shown, for example by Sir William Hamer, Dr. Crookshank, and our president, Dr. Goodall. Other external factors must participate in the genesis of epidemic diseases, particularly meteorological factors. This is a revival of the Hippocratic *catastasis*, which was developed by Sydenham, although inadequately translated as "epidemic constitution". From a more philosophical point of view it consists in consideration of all modifications of the macrocosm.

Causalism was demonstrated as insufficient also because it failed to take into consideration a series of important ætiological factors, the factors of resistance of the body which are summed up in the term diathesis or predisposition. Professor Ryle has defined diathesis as a transmissible variation in the structure and functions of the tissues rendering them peculiarly liable to react in a certain way to certain extrinsic stimuli. I would prefer to widen the definition, and to understand by diathesis a hereditary or acquired, transmissible or non-transmissible variation in the structure or function of the tissues rendering them peculiarly liable to react in certain ways to certain external stimuli.

Diathesis or predisposition depends on the psychophysical make-up of the individual, in other words, on his constitution. This is why we can consider diathesis and constitution as practically synonymous. Constitution means the psychophysical make-up of the organism. Diathesis mean the psychophysical make-up of the organism in relation to its disposition to disease.

The first conception to be developed was the following: Men differ. Each has his own psychophysical make-up, a special constitution. Every man therefore responds differently to external noxious agents and thus develops disease differently from another. In considering the genesis of disease we must therefore consider the special constitution of the patient which may include a special diathesis or disposition.

This conception is an important element in Hippocratic medicine. In the nineteenth century, however, principally after the advent of bacteriology, it was almost discarded. Only the external factors were considered and little attention was paid to the special disposition of the individual patient. Revival of interest in constitution, diathesis, or temperament dates from the late seventies. It started simultaneously in France, England, and Italy, and spread a little later to Germany.

In France it began with the introduction into the Paris school of the Hippocratic conceptions of the Montpellier school by Emile Chauffard, who became professor of general pathology in the seventies. It was developed by Bazin and principally by Charles Bouchard, who succeeded Chauffard in the chair of general pathology.

French workers have played an important role in developing the Hippocratic idea of the role of the diathesis in disease, but as their point of departure was essentially clinical they did not make a clear distinction between diathesis and the disease itself.

In England the importance of the constitution in the ætiology of disease was introduced by Thomas Laycock, but mainly through the work of Jonathan Hutchinson, who exposed his ideas in *The Pedigree of Disease* (1881). The British work is based on more biological principles and linked up with the ideas of Darwin and Galton (Hutchinson dedicated his *Pedigree of Disease* to Darwin). For this reason the distinction between diathesis and disease is made clearer. In Hutchinson's work the difference between man and man is set forth distinctly, and "this difference proves of much importance in modifying the process of disease". The publication of Hutchinson's lecture stimulated interest in diathesis, and its role has been dwelt on by many later writers such as Sir Archibald Garrod, Sir Walter Langdon-Brown, Professor John Ryle, and Dr. Maitland Jones.

In Italy the idea of constitution was introduced into the conception of ætiology of disease by da Giovanni, who first published his work in 1878. Since then it has been further developed by a series of brilliant workers, among the foremost being Viola and Pende.

In Germany the constitutional ætiology of disease was introduced by Beneke, whose first published work on the subject dates from 1878, but the idea gained ground but slowly. Not until 1892 did interest in the constitution revive, with a paper by Hueppe, a bacteriologist, who showed the inadequacy of bacterial causalism for the understanding of infectious diseases and insisted on the importance of the soil, of diathesis, as an ætiological factor. After Hueppe came Martius, whose first book on the ætiology of disease and predisposition to disease was published in 1898, and who developed constitutional ideas during a long life of teaching and work, ploughing a lonely furrow in a small university town. The ideas of Martius, however, ultimately triumphed. Constitutional conceptions were taken over by Kraus and Brugsch, by Kretschmer in Germany, and by Bauer in Vienna, and Naegeli in Zurich.

Another series of researches was devoted to an attempt to discover the nature of the constitution.

In a first phase the morphological point of view was developed simultaneously by Beneke in Germany and da Giovanni in Italy. The differences between man and man—between constitutions or biotypes, to use Pende's terminology—were mainly morphological. As da Giovanni put it, "the cause of the special morbidity of an organism resides in its special morphology". This view was developed in Italy by Viola, in France by Sigaud and his pupils, in Germany by Brugsch, and in America by Draper.

In a second phase the biochemical or metabolic point of view was developed. According to this conception the difference between individuals (and thus the difference between disposition to disease) is chemical. This view was emphasized in France by Bouchard and Albert Robin, and crowned by the work of Sir Archibald Garrod, who in his *Inborn Errors of Metabolism* developed the idea of chemical individualism.

In a third phase is developed the point of view which can be called integrative or enlarged endocrinological. This is the modern point of view and was emphasized at the recent "settimana medica" at Salsomaggiore devoted to constitutional medicine. The principal work on this subject has been contributed by endocrinolcgists, predominantly by Pende, who has detached himself from the exclusive morphological view of the Italian school and considers that constitution or biotype means a special mode of functioning of the endocrines and vegetative nervous system, the great regulators of constitution. Working on parallel lines I have developed a conception based on the British work on integration. Our constitution, our psychophysical make-up, our biotype, is regulated by the integrative system of the body, the psycho-neuro-endocrine system. A special constitution and thus a special

diathesis means a special mode of functioning of endocrines, vegetative nervous system, and psycho-associational cortex, a special modality of psycho-neuro-endocrine equilibrium.

The biological or constitutional principle of treatment consists in treating a diseased individual by helping, sustaining, his constitution to fight the disease.

It consists thus in adopting those therapeutic agents which clinical experience and physiopathology have proved efficacious in strengthening the constitution in its struggle to recover equilibrium. The object, according to this principle, is not the local disease but the constitution, and action is directed towards the regulators of constitution, the psycho-neuro-endocrine system.

This principle is in opposition to the nihilistic and the chiracistic principles of therapeutics.

The nihilistic principle, which consists in doing nothing and letting Nature pursue its course, found its most complete expression in the Viennese anatomo-clinical school during the mid-nineteenth century. It was made possible by the violent chiracistic procedures of the physicians of that time, who delighted in excessive bleedings and strong doses of toxic drugs that did more harm than good. The physicians of Vienna found that patients fared better when left alone. Another trend of thought leading to therapeutic nihilism was excessive reliance on the *vis medicatrix naturæ*. If Nature be the only physician then let us not interfere. There are two sorts of disease, those which Nature is incapable of curing and will therefore prove fatal despite medical intervention, and those which Nature can cure and therefore need no external help. The Viennese summed up this conception in a cruel phrase : "There are no good or bad physicians, but simply lucky or unlucky physicians." The best thing that patients could expect in the Vienna of those days was to be diagnosed by Skoda and autopsied by Rokitansky.

The chiracistic principle, so called from Chirac, the French eighteenth-century physician and one of its leading exponents, consists in excessive intervention. Chiracism is in absolute opposition to Hippocratism, and is based on the mechanistic conception of disease. According to the Chiracists, who include the Rasorians, the Broussaists, the Brownians, disease results from the mechanical action of external factors or stimuli. There is no special curative reaction of the body. To cure disease we must therefore mechanically apply stimuli contrary to those that have provoked the disease. The Chiracists are characterized by their contempt for the ancients, meaning Hippocrates. Their principle resulted in immoderate bleedings, excessive administration of antimony, and other violent drugs. It is to be noted that the Greek mechanists, Asklepiades, Themison of Laodicea, Thessalos of Tralles, although in theory akin to the Chiracists, possessed the Greek sense of measure and therefore did not allow their theories to lead them to violent and blind interventions. In their practice they were Hippocratists. Even Themison and his pupils, who developed metasyncrisis or shock treatments, were animated by a biological and clinical spirit.

Recent clinical work has shown that of these three principles the constitutional or biological principle has a greater pragmatic value. And to this principle is due the great progress in therapeutics and development of the constitutional methods of treatment.

Constitutional thinking has helped development of psychotherapy. The psycho-associational cortex belongs to the system of integration of the body. It is in fact the summit of integration. The psycho-neuro-endocrine system is the system that fights against external morbid elements. Thus by reinforcing the psyche by means of psychotherapy we obtain therapeutic results through the mechanism of constitutional treatment. Psychotherapy is a major biological or constitutional treatment, and its significance has been enhanced by the recent demonstration of the physiological connexion between psycho-associational cortex, vegetative nervous system and endocrines, and thus between the psycho-associational cortex and all organs and tissues of the body.

Dietotherapy, which looms so large in Hippocratic medicine, also has been developed on biological or constitutional lines. The aim of modern dietotherapy is the strengthening of the constitution, and to do this we look at the whole man and not at a diseased organ. In chronic nephritis, for example, until a few years ago the object was to spare the kidney, and thus we reached the method summarized in the saying of a French clinician, " Le lait ou la mort ". Nowadays we look on the whole man and endeavour to improve his constitution by giving those elements of nutrition which qualitatively and quantitatively maintain his strength.

The wonderful development of physical medicine, in which this country has been so prominent, is another manifestation of constitutional thought in therapeutics. Physical methods do not cure arthritis or nephritis or nervous diseases as diseases, but they improve the constitution and thus help the patient to fight his disease.

Pharmacotherapy has been modified markedly according to constitutional conceptions. The haphazard and empirical use of drugs had resulted in the drug nihilism of our immediate predecessors summarized by Oliver Wendell Holmes when he said that if all drugs were thrown into the sea it would be so much the better for humanity and so much the worse for the fish. Drugs have come into the foreground again but are now being used on quite different lines.

In the introduction of endocrine products as drugs we find an essentially constitutional procedure. Through it we act on the basis of constitution. Chemotherapy also has advanced since introduction of the constitutional outlook into its practice.

The constitutional outlook in therapeutics has contributed to renascence of the old alterants, purges, and other drugs which our ancestors used to purify the humours and to soothe the nervous system. Disintoxication and nervous sedation by these means put the patient in better condition to fight his disease and through these general means, as Aschner has shown, many local diseases can be treated. Aschner, whose work marks an epoch in the history of Neohippocratism, has developed this mode of constitutional therapy in a series of publications that have had great success in German-speaking countries. He reintroduced the alterants, laxatives, and nervous sedatives used by our ancestors, chiefly by Paracelsus, and has obtained good results in gynæcological affections and in other local diseases. The only criticism I have to make is that the methods used by Aschner are part of constitutional therapy and do not form the whole.

One of the most interesting elements of the introduction of the constitutional outlook in therapeutics is the attention paid by some Neohippocratists to homœopathy. This interest was kindled by the Neohippocratists Bier and Hans Much. It must not be forgotten that Hippocrates wrote in a famous passage that "There are diseases to be treated by similars, others better treated by contraries. Everything depends on the nature of the disease ". It must not be forgotten also, that throughout the Chiracism of the late eighteenth century and the localistic tendencies of the nineteenth century the homœopaths maintained the constitutional outlook.

The problem is complicated because Hahnemann—without doubt one of the great physicians of the ages—in fact introduced three separate principles, the principle of *similia similibus*, the principle of constitutional catalysis, and the conception of minimal doses and of drugs transformed into a state akin to a colloidal condition. The principle of homœotherapy, according to which a drug in small doses cures a morbid condition similar to that produced by the same drug-poison in a higher dosage, has been demonstrated as true. It has been found to tally with the technique of collateral desensitization. Knowledge of constitutional catalysts, that is, of drugs suited to and acting on a special constitutional type (the homœopathic polycrests, artificially included with the *similia similibus* principle) has been confirmed by modern science. The action in certain cases of drugs in minimal doses has also been confirmed by modern scientific work, and in endocrinology we obtain results with doses akin to the medium potencies at least of the homœopaths. Modern

physico-chemical research and knowledge of colloids have further developed Hahnemann's principle of drug dynamization.

Thus the basic principles of homœopathy are in accordance with modern scientific work, and Hahnemann can be considered as a great scientific pioneer. The application of his principles in medicine, however, is far from perfect, as demonstrated by the chaos that reigns in the practice of the homœopaths themselves, who are divided into numerous schools. The conclusion of the Neohippocratists formulated by Delore of Lyons in his *New Tendencies in Medicine* is that homœopathic procedures have their particular indications, but that before we introduce homœopathy into the body of general medicine the experimental basis of the homœopaths must be subjected to precise scientific work. At present the clinical applications lack this, through no fault of the homœopaths, who have always been excluded from the centres of scientific research. On the whole there seems to be a great deal of truth in homœopathy, and this method is effective, although in limited and well-defined cases.

Scientific study of the therapeutic methods based on the work of Hahnemann, determination of their precise indications, and their introduction into general medical practice, can only benefit and enrich our therapeutic armamentarium. This is especially evident from the fact that homœotherapy is an excellent method of collateral desensitization, and recent work has shown that sensitization is a potent factor in the chronic diseases so frequent to-day. We must remember the words of the great Trousseau, " La clinique prend son bien partout ou elle le trouve ".

To this attitude of Neohippocratism the homœopaths have reacted variously. Those who maintain homœopathy as an exclusive method and the *similia similibus* as a universal law are somewhat sceptical. On the other hand a whole group of French homœopaths have accepted the Neohippocratic doctrine with its limitation of homœopathy to certain well-defined cases and its postulation of the need for a more scientific elaboration of the principles of Hahnemann.

Surgical indications have also been modified in the light of the constitutional outlook. Certain modern surgical procedures such as intervention on the vegetative nervous system and on the endocrines are general constitutional procedures. This biological point of view is well developed in the works and lectures of Professor Leriche of Lyons, the pioneer of vegetative nervous surgery. Altogether, however, the indications for surgery are diminishing because through action on the constitution results are obtained in local conditions which some years ago were the exclusive domain of surgery. This is particularly marked in gynæcology, where operations have greatly decreased thanks to the introduction of general constitutional methods, principally psychotherapy, physical medicine, and endocrinotherapy. Mohr in his *Psychotherapy in Organic Disease*, reports that a well-known gynæcologist reduced his operations by 50% since having recourse to psychotherapy. Even this proportion gives promise of further reduction thanks to the introduction of endocrinotherapy, as the internist endocrinologist Maranon shows in his *Gynecologia Endocrina*.

The Neohippocratic Doctrine and Medical Practice

I have attempted to show that the fundamental principles of the Neohippocratic doctrine—the organismal principle, the principle of the holistic nature of disease, the principle of the ætiological constellation and the principle of constitutional treatment —have been given scientific demonstration by the work of the last twenty to thirty years. How can these principles be applied in practice ? How is the modern, the Neohippocratic, physician, to approach the patient ?

The practice of the Neohippocratic physician consists in triple act of diagnosis —diagnosis of the patient, diagnosis of the disease, diagnosis or choice of remedy.

Diagnosis of the disease, the labelling of the patient, is important as a " safety first " diagnosis and is a stepping stone to the complete diagnosis.

Diagnosis of the patient, diagnosis of the person, is the basis of Neohippocratic practice. For each individual patient we have to consider first the factors, external

and constitutional, that have brought about his morbid condition, making a complete study of the conditions which may have led to the result. Next we have to investigate the mode of functioning of his integrative system, psyche, vegetative nervous system, and endocrines. Lastly we have to consider all functional disturbances and lesions of his organs. The technique of this diagnosis, consideration of the four panels of personality—ætiological, physical metabolic, mental, and organic—has been developed in my previous publications.

Diagnosis or choice of remedy comes next, and is based exclusively on diagnosis of the person. The problem to solve is how to help the patient, how to help the psycho-neuro-endocrine system of the patient, to combat his disease. For this purpose we must choose without bias from all therapeutic agents, psychical, dietetic, physical, pharmaceutic, and surgical. In this choice, following the old Hippocratic principles, we must take as basis not systems or schools, but purely clinical experience. Thus we must avoid a dogmatic attitude in choice of drugs and, according to the clinical indications, we must employ endocrine preparations, chemotherapeutic agents, vaccines and sera, physiological remedies, and homœopathic remedies.

It is plain from this attitude that Neohippocratism does not consist in the introduction into medicine of " a little less science and more art ", to use the words of Trousseau. Neohippocratism introduces *more art and more science*.

An important element in the contemporary practice permeated by Neohippocratic tendencies is our attitude to specialties. Neohippocratic medicine is a holistic medicine, but in practice specialties have been shown to be essential. The problem is not so great for surgical specialties, for being specialties of technique they are completely justified. The problem is much greater for medical specialties such as neurology, cardiology, endocrinology, gastro-enterology, dermatology, and others. In these specialties the technique is diagnosis and internal treatment, and diagnosis and internal treatment are both only of the whole, or constitutional.

There is a tendency nowadays even among ardent Neohippocratists, to maintain these specialties but to introduce into their practice the constitutional outlook. Professor Laubry, when inaugurating the chair of cardiology in the Faculty of Medicine of Paris, said that the modern specialist is a physician who sees the whole from a particular point of vantage. This definition is far better than the classical one of the physician who knows more and more about less and less. The modern specialist can work on Neohippocratic lines if to his proficiency in local exploration of one system he adds the capacity for making a perfect " diagnosis of the person ".

The contemporary Hippocratic movement is but one of a series of recurrences of Hippocratism. At all periods of its existence medicine has turned to Hippocratic principles whenever intense analytical work or dogmatism was hampering its progress. Areteus and Galen turned medicine back to Hippocrates when it was submerged by the analytical physiological work of the Alexandrians. In the Middle Ages Rhazes and Maimonides guided medicine back to Hippocratism to save it from the routine originating in the false interpretations of Galen. Thomas Linacre and the first presidents of the Royal College of Physicians also directed their work along Hippocratic lines to help medicine to emerge from the scholasticism of the Arabizing physicians of the Middle Ages. Sydenham reintroduced the Hippocratic spirit of clinical research against the intense dogmatism of the sixteenth and seventeenth century schools. Hahnemann also attempted a Neohippocratic movement, at all events in therapeutics, although the spirit was unfortunately stifled as it became a dogma.

The contemporary Neohippocratic movement originated as a reaction from the intense analytical work of the nineteenth century. During the nineteenth century medicine developed like a tree that produces luxuriant foliage and rich fruit without allowing the roots to grow at the same time. Its growth became artificial, and, like the giants of the forest, could be shattered by the wind. Neohippocratism consists in return to the development of the roots of medicine. The watchword " Back to Hippocrates " indicates return to the spiritual values of Hellenism.

Section of Neurology

President—ANTHONY FEILING, M.D.

[*October* 21, 1937]

Central Pain in Spinal Cord Lesions

PRESIDENT'S ADDRESS

By ANTHONY FEILING, M.D., F.R.C.P.

IT seems desirable in the first place to define what is to be understood by the term "central pain". By common consent this term is generally restricted to pain occurring from lesions in the substance of the central nervous system in which, as regards cerebral lesions, the possibility of the pain being produced by a general rise of intracranial tension can be excluded. Obviously also those cases are excluded where the pain may be caused by lesions of the meninges or by involvement of the afferent neurones outside the brain or spinal cord, such as lesions of the cranial nerves, spinal nerve-roots, or posterior root ganglia.

It has of course been known for many years that the substance of the central nervous system, both white and grey matter, is very largely insensitive to pain from direct injury such as cutting or bruising, and this knowledge has no doubt been responsible for the somewhat tardy recognition of the existence of "central pain".

During the last fifty years, however, many valuable contributions to this subject have been made, especially in regard to pain from lesions of the optic thalamus and brain-stem. It would be an unprofitable task to attempt in one brief address to cover the whole of this subject, and I am confining my remarks therefore to central pain in association with lesions of the spinal cord, an aspect of the wider problem of central pain in general which has probably attracted less attention than it deserves.

Transitory pains may, of course, occur in a very great variety of spinal cord lesions, but it is with pains of a more persistent character that I am concerned, and it will be found that the cases of real central pain exhibit three chief features in regard to the pains: (1) That they are spontaneous, (2) that they are persistent, and (3) that their distribution is more or less fixed or constant in each individual case.

The subject may be considered under the following heads: (1) Injuries of the spinal cord, (2) tumours of the spinal cord, and (3) certain intrinsic diseases of the spinal cord especially syringomyelia, disseminated sclerosis, combined degenerations, and cases of vascular disease.

INJURIES OF THE SPINAL CORD

Persistent pains of the kind with which I am dealing are not common in spinal-cord injuries. But they are to be encountered from time to time both in cases of injuries in warfare and also in the ordinary injuries of civil life. Striking examples were found in certain cases of spinal injuries in the Great War. Of these Holmes

(1919) has given a valuable account. He noted that in all cases the pains were spontaneous but were apt to be much aggravated by any external stimuli, even by light contacts and particularly by movements of the affected parts or by any vibrations. The pains were very often referred to areas supplied from the seat of the injury, thereby raising the question whether such pains were not due to injury of the posterior roots or posterior root ganglia, but that this explanation could not be correct in all cases was proved by his experience of numerous cases where severe pains of the same character were referred to distant parts below the level of the wound. Hyperæsthesia tended to accompany the pain in all cases and was more persistent than the pain itself. The severity of the pain generally tended to abate in from two to three weeks. In cases of unilateral injury to the spinal cord he found that the pains were felt chiefly on the paralysed side. In agreement with other observers of similar cases Holmes noted that central pains of this type occurred most frequently when the injury was in the cervical part of the spinal cord.

Central pains of this type may occur from severe concussion or commotion effects upon the spinal cord without any direct external wound of any kind. A typical case of this kind and the first that I saw during the Great War made a lasting impression on my mind.

On May 17, 1915, a young officer was blown up in the air by a high explosive shell; after he fell a second shell exploded near him. Although he received no actual wounds, there was immediate paralysis of both arms and legs and very severe pain in the hands and arms. There was retention of urine for three days only, and the legs rapidly began to recover their power. Examined on June 1, all voluntary power had returned to the legs, where no abnormal signs could be found except a double extensor plantar response and some diminution of the sense of vibration. The outstanding features of the case, however, were intense pain and hyperæsthesia in the arms and hands. He lay perfectly still in bed with the arms motionless across his chest. On my approaching, he exclaimed "Whatever you do, for God's sake don't sit on the bed or shake it". He complained bitterly of constant and severe pains in the hands and arms, especially along the ulnar borders; these pains were greatly aggravated by any movements or by any sudden jarring of the body. The arms could be moved quite freely from the shoulders, but it was impossible to get him to move his hands on account of the pain. There was no gross loss of sensation, only a hypo-algesia to a pin-prick in the 8th cervical and 1st dorsal root areas, but in spite of this hypo-algesia there was an intense hyperæsthesia to all light contacts. These symptoms gradually diminished in severity, but it was not until five months after the injury that recovery was complete.

Although it is unusual to find in the spinal injuries of civil life examples of central pain so striking as these, yet we often discern minor examples of the same nature. My own experience has been that such cases are nearly always confined to injuries of the cervical part of the cord, where severe pains are often referred to the arms, especially in the distribution of the 8th cervical and 1st dorsal segments. In these cases also hyperæsthesia may persist for some time as a troublesome symptom. Lhermitte (quoted by Ajuriaguerra, 1937) in a communication to the First International Neurological Congress in 1931, brought forward a valuable contribution dealing with the sensory disturbances following spinal cord injuries. Besides the type of pain just described, which he agrees in finding most common in cervical injuries, he distinguished other forms which are less common, thus, hyperalgesia to cutaneous stimuli without spontaneous pain, pains of a character like electric shocks provoked by movement and pains of a type recalling those of tabes.

One striking fact emerges from my own experience of these cases in general, and that is that the more severe the spinal injury the less is the likelihood of the occurrence of central pains. They must be very unusual, if not unknown, in cases where paraplegia is complete for any great length of time, but yet they do not appear in cases of the slightest degree of spinal injury which evince only a very transitory paralysis. A moderate degree of damage to the cord short of complete interruption of function appears to be the lesion which allows these pains to arise.

Tumours of the Spinal Cord

Pain is of course a well-recognized early symptom in tumours of the spinal cord. The most characteristic type of pain is the root pain of segmental distribution occurring in extramedullary tumours. After that the most common type probably is pain in the back, referred to the spinal column and generally central in situation. This form of pain is perhaps most often found in cases of tumours affecting the lower part of the spinal cord, especially the lumbar region, and is recognized as being particularly marked in cases of extradural malignant disease. With these pains I am not particularly concerned, but wish rather to draw attention to pains of a quite different kind which in my opinion occur more frequently both in cases of extra- and intramedullary tumours than is commonly believed. These are pains referred to distant parts and in areas not supplied with sensation from the nerves at the level of the lesion.

Although many observers have drawn attention to the occurrence of these pains, they hardly seem to have received the attention which they deserve. Horsley (1911) refers to the frequent occurrence in cases of compression paraplegia of pain being referred to parts some distance below the lesion. Elsberg (1925) too has emphasized the importance of this kind of pain, and in the literature of the subject many examples are to be found. I have myself observed several cases of this kind in which the earliest complaints were of pain felt in the legs, not of a radicular type, and most often referred to the distal parts of the legs, and in cases where a tumour was present in the cord some considerable distance above the lumbar region.

Thus in one case of an elderly woman who exhibited spastic paraplegia with no clearly defined loss of sensation and in whom the diagnosis of a lateral sclerosis had been upheld for some time, I noted that she had always complained of persistent aching and boring pains in both legs, of which, she rather pathetically remarked, "little notice had been taken". Eventually a lipiodol injection into the cisterna magna revealed the presence of a partial block in the cervical region and operation disclosed an intramedullary tumour of the cord extending over an area from the 7th cervical to the 1st dorsal segments at least.

A good example of an extramedullary tumour in which persistent and severe pains were referred to distant parts is that reported by Parker (1930) in a woman, aged 51, with paraplegia and anæsthesia up to the 9th dorsal segment, who suffered from severe and persistent pain in both legs. At operation an extramedullary meningioma at the level of the 6th and 7th dorsal segments was found and removed, with complete cure of both the paraplegia and the pain.

Occasionally intramedullary tumours of the spinal cord may produce most intense and persistent pains widely distributed and very intractable. A remarkable example of this was the following case under my own care a good many years ago.

It was that of a man, aged 35, suffering from loss of power in all four limbs and severe and persistent pains in the limbs and trunk. The symptoms had begun with numbness of the right hand ten years before; five years later pain had been noticed between the shoulders and extending down the right arm. Some three years before I saw him paraplegia gradually set in and a year before weakness of the arms had appeared. The pain which had begun in the right arm gradually spread to the right side of the trunk, then affected the right leg, and later involved the left side of the body from below upwards. When I first saw him he showed an almost complete motor paralysis of both arms and hands, with slight muscular wasting, a very severe spastic paraplegia and a gross impairment of all forms of sensation below the 4th cervical segment. For my present purpose, however, the most interesting feature of his case was the pain. This was spontaneous and constant and felt all over the body except in the head and neck; this pain was also subject to exacerbations which were nearly always to be provoked by movements of the limbs or any rough handling of them. The constant pains, which were described by the patient as vibrating pains, altered in character with the spasms or exacerbations to a sensation "like knives" or "as if he were being cut into ribbons". At that time he needed at least three grains of morphia in the day

to keep him in a state even of tolerable discomfort. Operation was performed in this case by my colleague Mr. Bankart. After removal of the 3rd to the 6th cervical laminæ the spinal cord was seen to be enlarged and unduly firm with adhesion of the arachnoid membrane to the cord. An incision was made into the postero-median septum and it was then noticed that the cut surface of the cord was unusually firm and yellowish in colour. The pain was unfortunately not relieved by this manœuvre. The patient died some three months later, the pain continuing and calling for increasing amounts of morphia for its relief.

There was never any possible doubt of the reality of the pain experienced by this unfortunate man. Observation of him left on my mind an impression of constant suffering as great, I think, as any I have witnessed.

Syringomyelia

The well-known and striking type of sensory loss so characteristic of syringomyelia has tended to produce a conception of the disease as one in which all sensations of pain are absent. Indeed outside purely neurological circles the occurrence of pain in this disease seems to be hardly recognized at all. I am far from claiming that severe pains are at all common, but there certainly exists a small proportion of cases in which pain is a predominant symptom. This fact is attested by many authorities, thus Gowers (1892) says " spontaneous sensations are common . . . in some cases pains " ; Oppenheim (1911), " pain is a not unusual symptom " ; Schlesinger (1902) remarks " pain may be intense " ; Raymonde and Lhermitte (1906) and Spiller (1923) have made valuable contributions to the same effect. Collier (1929) says that " there are notable exceptions to the general experience that syringomyelia is a painless disease". A study of a number of reported cases and a small experience of my own lead me to believe that pain may be an early symptom. The description of the character of the pain varies ; such word pictures as burning, like knives, and occasionally painful sensations of cold are to be noted. In the majority of cases the pain is referred to areas which are innervated from the cervical and upper dorsal regions of the cord only. The shoulders and arms are most affected, and frequently the upper part of the thorax. Although both sides of the body may be affected, in some cases at any rate the pain may be entirely unilateral. In those cases where the pains are confined to the upper extremities and the trunk it has generally been found that a hypo-algesia and loss of diminution of thermal sensibility has co-existed in the areas in which the pains are felt. Cases are on record, however, in which persistent pains have been referred to the legs. Spiller (1923) has recorded such a case with autopsy ; a coloured woman presented signs and symptoms of syringomyelia with the addition of severe pains in both legs. At post-mortem a typical cavity was present at the level of the 7th and 8th cervical segments and extending down as far as the mid-thoracic region ; no sign of the disease, however, was present in the lumbar part of the spinal cord. Ajuriaguerra (1937) states that in one of his cases the onset of the disease was heralded by abdominal pains which suggested at first the diagnosis of appendicitis. He has also remarked on the frequency with which pains have affected one side of the body only.

I have had under my care for the last seven years a very typical example of the painful form of syringomyelia.

The patient is a man now aged 42, whose disease was ushered in seventeen years ago by severe pains in the left shoulder and supraclavicular region extending into the left upper arm and the left side of the thorax down to the nipple. It was apparently not until at least two years later that he appreciated some weakness of the left hand and arm. His condition when I first saw him comprised, in brief, a paresis of the left cervical sympathetic with hyperidrosis of the left side of the face and neck, analgesia and therm-anæsthesia over the left side of the face, the left arm and hand, and left side of the chest as far as the 4th dorsal segment ; slight muscular wasting and weakness of the left hand and forearm, loss of the tendon jerks in the

arms, spastic paresis of the left leg with exaggerated knee and ankle jerks on both sides and double extensor plantar responses. He complained of constant pains in the left shoulder and arm and side of the face; he described these as an ache, and said that at times the pains became aggravated especially by the cold and were then "like knives". The pain was not provoked or increased by movement nor by stimulation of the skin or muscles. He has never had pain on the right side of the body. These pains have persisted over the whole of the last seven years, but have undoubtedly diminished in severity, possibly as the result of the X-ray treatment he has received.

Although such a reference is really outside the scope of my paper, I may just recall to you the well-recognized existence of severe trigeminal pain in syringomyelia, pain indistinguishable from that of ordinary trigeminal tic.

It has often been considered that the pain in syringomyelia is due in some way to distension of the cavity or cavities in the spinal cord. Such a theory is attractive but difficult to establish with certainty. It is undoubtedly a fact that in some cases of syringomyelia submitted to operation the cord has been found much enlarged and distended. Hassin (1920) records a case in which at operation the distended cord completely filled the theca and did not pulsate. And there can be no doubt that a state of increased fluid pressure within the cord may exist. Collier (1929) speaks of those cases "in which the distension of the cervical spinal cord is so great as to cause that structure to press upon the bones of the spinal canal", and considers that "constant and intolerable pain may result necessitating surgical interference for the relief of the pressure". The results, however, of surgical operation for the relief of the pain have been far from uniformly successful. Moreover, a gross enlargement of the cord has been found at operation in cases in which pain had been absent. I am not cognizant of many observations made on the pressure of the cerebrospinal fluid in syringomyelia as revealed by ordinary lumbar puncture nor of many recorded increases in the protein content of the fluid which might suggest some subarachnoid block. In the first personal case I have already quoted two such observations were made, and it is interesting to note that on the first occasion the percentage of protein in the cerebrospinal fluid reached the abnormal figure of 0·07%, while on a later occasion the amount of protein was quite normal. And yet there was no difference in the amount of pain of which the patient was complaining at these different times.

My own conclusions at present are that when severe and persistent pains occur X-ray treatment is the first method of choice, and if this fails to relieve the pain operation may then be considered. The exact type of operation to be carried out is still a difficult matter to decide. Simple incision of the cord has, I believe, been generally followed by a return of the pain at no very distant date; probably more success may be hoped for from the operation of completely dividing the cord in the middle line over a number of segments, thereby ensuring that the fibres crossing the middle line and carrying sensations of pain will be divided.

Disseminated Sclerosis and Subacute Combined Degeneration of the Spinal Cord

These two conditions may be considered together in regard to the question of pains, for in both, similar types of subjective disorders of sensation may exist. Of course paresthesiæ of every description are common in both diseases and are recognized as early symptoms, although in the case of subacute combined degeneration they are apt to be more persistent and more prominent. They assume every conceivable form—numbness, tingling, formication, sensations of swelling or constriction or of tight bands and girdle sensations, all of which may affect both the limbs and the trunk. Less often, and then much more commonly in my experience in subacute combined degeneration, peculiar thermal dysæsthesiæ are to be found, especially a sensation of intense cold. For some reason which I cannot explain, sensations of heat or warmth are very unusual.

It is not always easy to draw the line between what should be termed a pain or a dyæsthesia. But although real pains of obvious severity are, I think, uncommon in both conditions, they nevertheless undoubtedly occur. In disseminated sclerosis they are most often found as an early symptom affecting especially the legs. They are spontaneous but not continuous, occurring as a rule in paroxysms spread over the course of a few days ; they are variously described as aching, like toothache, or sometimes like electric shocks ; not very infrequently pains of a nature and distribution resembling sciatica are to be found. Rarely girdle pains of considerable severity and persistence may occur. In one personal case the symptoms were so suggestive of a spinal tumour as to lead me to advise laminectomy, but the subsequent history of the case proved, I think, that it was one of disseminated sclerosis. I may add that this was in the days before the introduction of lipiodol.

A man aged 38 began to suffer from pains round the lower ribs on the left side; they were persistent and severe and were much aggravated by violent movements and sneezing or coughing. Some six weeks later weakness of the left leg appeared. On examination he showed a gross spastic paresis of the left leg and slight weakness of the right leg; both knee-jerks and both ankle-jerks exaggerated and a double extensor plantar reflex. There was loss of sensation, especially for pain and temperature, as high as the 5th dorsal segment the loss being most marked from the 6th dorsal to the 1st lumbar levels. There was a slight excess of protein in the cerebrospinal fluid, 0·06%, but otherwise no abnormality.

No tumour was found at operation. The symptoms gradually improved and all the pain slowly disappeared ; some eighteen months later, however, a feeling of numbness with slight muscular weakness and inco-ordination appeared in the left arm, to disappear again in the course of a few months.

Although reference to affections of the brain-stem is, strictly speaking, outside the scope of this paper, I may perhaps recall to your notice the occurrence of severe trigeminal pain in disseminated sclerosis. Harris (1937) has recorded an experience of 45 examples of this association, in which the trigeminal pain was bilateral in 7 cases. Oppenheim (1911) and Marburg (1909) have each recorded a case in which pathological confirmation of the causal lesion was found in the form of a plaque involving the fibres of the 5th nerve at their entrance to the pons.

In subacute combined degeneration girdle sensations and pains are not very uncommon, and in quite a number of cases severe pains in the legs may be complained of. For the latter, however, we must be cautious in assuming a spinal-cord origin, since it has been conclusively established that degenerative changes occur in the peripheral nerves.

Some of the most obstinate cases of central pain from affections of the spinal cord that I have personally encountered have been in cases in which a diagnosis of vascular lesions has been made, I believe on sufficient grounds. These cases have been in middle-aged or elderly persons, the subjects of obvious arterial disease and nearly always with considerably raised blood-pressure, in whom every care has been taken to exclude syphilis and in whom the passage of time as well as clinical examination has served to exclude any other diagnosis. I will quote briefly two such cases.

I.—Four years ago a lady aged 61 consulted me on account of pains in the lower part of the legs and feet and a sensation of intense freezing cold in the feet. The pains were practically continuous, of a cramping kind and were quite unrelieved by any change of position and bore moreover no relation whatever to exercise ; indeed they were often much worse in bed. Abnormal signs were present in the nervous system, absence of the right knee-jerk and a very sluggish left knee-jerk, absence of both ankle jerks and double extensor plantar reflexes. No objective loss of sensation except a diminution of vibration sensibility in the distal parts of the limbs. Blood-count normal. Good pulsations in the posterior tibial and dorsalis pedis arteries and no evidence to suggest that the pain was due to disease of the peripheral arteries in the legs. Wassermann reaction negative. Palpable vessels considerably thickened, with a B.P. of 195/110. Every kind of local treatment to the feet and legs had been tried and at the end of four years the symptoms are still unrelieved. I can find no explanation to account

for these symptoms and signs except a local myelopathy in the lumbo-sacral part of the cord, presumably some degeneration from arterial disease.

II.—A good example of central pain from a myelopathy probably dependent upon vascular thrombosis was that of a man aged 52, first examined two years ago. Three months before he had noticed tinglings in the fingers of both hands and a month later burning pains were felt in the left and then in the right leg; a little while after there occurred a sudden onset of severe pain in the right upper extremity from the shoulder to the tips of the fingers. Six weeks after the onset of this pain he presented the following picture : marked weakness of the right arm with slight muscular wasting of the small muscles of the hand; fibrillation in the deltoid and flexors of the forearm; some ataxia of the right arm; active tendon-jerks in both arms, spastic paresis of the legs, greater on the right side with exaggeration of both knee-jerks and both ankle-jerks and a double extensor plantar response; diminution of sensibility especially for pain on both sides of the body as high as the 7th dorsal segment, more marked on the left side. Palpable vessels much thickened, with B.P. 185/100; Wassermann reaction negative; cerebrospinal fluid normal. The pain in the right hand was persistent and severe and the source of constant complaint for the whole of the next three months, nor did it entirely disappear for more than a year, although the motor paralysis and the loss of sensation both cleared up much more quickly. Even now two years after the onset of the illness the patient tells me that the right hand sometimes aches severely.

So far I have briefly discussed a number of conditions in which pain arises from lesions which are, without doubt, of the spinal cord itself. I must now refer to that condition which of all diseases of the spinal cord is most prone to exhibit striking and characteristic pains : I mean tabes dorsalis. You may perhaps be surprised to hear the suggestion that the pains of tabes may be related to central lesions, since different conceptions have for a long time attracted most attention, conceptions which would place the earliest lesions outside the cord in some part of the posterior nerve-roots. I hope, however, to convince you that there are some grounds at any rate for upholding a different opinion. Any satisfactory theory of the causation of the pains in tabes must take into account certain important facts about them. First their peculiar characters, which are chiefly as follows : They occur in bouts or paroxysms, sometimes almost daily and sometimes separated by weeks or months or even occasionally years. Each attack is not composed of a continuous pain but of a succession of sharp almost momentary pains which have, of course, given rise to the classical term lightning pains. These peculiar pains also are not distributed along areas supplied by peripheral nerves nor over root or segmental areas, but are felt in a more sharply localized area in many cases a small spot. They are often described as being like knives or needles piercing the skin perpendicularly to the surface. The second important point about them to which I wish to draw attention is their persistence, and the third point is that they often constitute the first symptom ; indeed they may precede all other manifestations by a matter of years. Finally, I would emphasize that these pains not infrequently continue when all other symptoms have improved and when pains-taking treatment has achieved a disappearance of a positive Wassermann reaction in the blood and when no changes are to be found in the cerebrospinal fluid.

Speaking of the method of production of these pains Gowers (1892) wrote as follows : "The long persistence of pains without any increase in the symptoms shows that they may be due to the action of structures that are changed but not changing". I am myself convinced that the persistence of these pains does not necessarily imply any progression of the disease.

The mechanism of these pains and their significance calls for a brief review of the histological pathogenesis of the disease, a subject over which much controversy has raged. While all observers are agreed that the essential lesion is a degeneration of certain of the exogenous fibres of the posterior root which enter the posterior columns, much difference of opinion has existed as to exactly where the disease process begins. At what point is the afferent neurone first attacked ? From the point of view of

the mechanism of the pain this is a crucial point since the pains are so often the first symptom.

The earlier theories propounded, particularly by Charcot and Pierret (1871), Strumpell (1882), and Spielmayer (1924), postulated a primary degeneration of the intramedullary fibres. Next came the theory of chronic meningeal inflammation causing pressure upon the posterior nerve-roots at their entrance into the cord; this was essentially the view of Obersteiner and Redlich (1894). Marie and Guillain (1903) and later Orr and Rows (1910), favoured the action of a syphilitic toxin on the posterior roots. Nageotte (1894) supposed that the first and essential lesion was an inflammatory change in the radicular nerve, and more recently Richter (1921) brought forward another explanation, that of the presence of a specific granuloma of the radicular nerve.

The theory of chronic meningeal inflammation constricting the posterior root loses much force from the facts that in many cases it has not been possible to demonstrate any marked meningeal changes, and that in cases of marked meningitis in other conditions such pains were not observed. Nageotte's theory fails to explain the absence of symptoms and signs referable to any involvement of the anterior roots which would surely be expected in at least a fair proportion of the cases. The work of Stern (1929) and others has thrown such doubt on Richter's findings and arguments that it is impossible, for me at least, to accept them. Finally, none of the theories which place the earliest lesion in any part of the posterior nerve-root seems to me particularly acceptable, since the characteristic pains of tabes are so unlike the pains which we are accustomed to associate with lesions of the posterior root in other diseases.

Stern (1929) has made a very valuable observation of degeneration discovered in the intraspinal part of the afferent neurone as early as three months after the onset of the first symptom.

My own inclination therefore is to revert to the earlier conceptions and to believe that the first changes occur in the intraspinal course of the nerve-fibre. This conception naturally leads to the conclusion that it is here that the impulses which give rise to the pains arise. And hence my submission that it is at least an arguable proposition that the classical pains of tabes with which we are all so familiar may be regarded as a form of central pain. Gowers (1892), from whose views on this subject I have already quoted, remarked that "the pains may reasonably be ascribed to the molecular changes in the nerve-fibres and their altered function either in the periphery or in the cord". We know of course that changes occur in the peripheral nerves, and it is therefore impossible absolutely to exclude their share in the mechanism of the pains. But it is so rare to find pains of the same character and persistence in other affections of the peripheral nerves that I find it difficult to accept such an explanation of their mechanism.

It now remains for me to try and draw some general conclusion and to set before you some suggestions as to the mechanism by which central pain may be produced in lesions of the spinal cord. We have seen that pains of different kinds occur in various diseases of the spinal cord itself in which it is difficult to find any constant pathological process which might be invoked as the essential causal factor. These pains have been found in the case of tumours, in syringomyelia, in disseminated sclerosis, in subacute combined degeneration, and in myelopathies dependent upon vascular disease. The only factor common to all these different conditions is an altered physical state of the nerve-fibres, of which many must be destroyed entirely and many be in a state of degeneration or slow death.

Two more general conclusions of importance which emerge are as follows: First, these central pains are referred in some cases to parts which are normally sensitive to objective testing of sensation, while in other cases they are referred to parts which are insensitive. Secondly, while the pains in some cases are referred only to parts innervated from the segmental level of the lesion, as ascertained by symptoms and

signs apart from the distribution of the pain, in other cases the pains are referred either solely or in addition to parts distant from the seat of the lesion.

It will be clear that afferent paths carrying sensation must be still functioning between the site of the lesion and the higher centres. The most natural explanation is to assume that the normal sensory pathway is in some manner stimulated by the altered state of the diseased nerve-fibres. The greatest difficulty in accepting this apparently simple explanation is the very long duration of the pains in many cases as well as our ignorance of exactly how such a stimulation may be produced. On the other hand it is undoubtedly true that nocuous stimuli directly applied to certain parts of the spinal cord can in fact produce pain. Thus Foerster (1927) produced pain by electrical stimulation of the antero-lateral funiculi, and Dusser de Barenne (1924) found that the local injection of strychnine into the posterior horns of the cord resulted in pain in the corresponding cutaneous areas.

While admitting that the conception of a permanent, or even long-standing, focus of irritation or stimulation is somewhat unsatisfactory, I still believe, myself, that it is on the whole the most probable explanation of these pains.

A different explanation that has been invoked to explain their pathogenesis is the theory that they are what has been termed a release phenomenon. This theory follows the work of Head and Holmes (1911–12), who from their studies of central pain in thalamic lesions, considered that the pain was a release symptom due to the removal of inhibition normally exerted through cortico-thalamic pathways.

A similar theory has been propounded by Foerster (1927) to explain the occurrence of spontaneous pains in spinal cord lesions. He believes that there exists a pathway from the cortex to an area in the lateral column close to the posterior horn which normally exerts an inhibitory effect on the pain-subserving functions of these horns : destruction of this pathway presumably therefore allows spontaneous pains to arise as a release symptom.

To me the truth seems to be that these theories of abnormal stimulation and of removal of inhibition are both conjectures, equally insusceptible of direct proof. Personally I find that hypothesis which would allow the existence of more or less permanent stimulation more acceptable than that of the removal of a normal inhibition.

Neither theory, however, seems to explain why in some cases of syringomyelia, for example, or if you will, of an intramedullary cord tumour, pain is entirely absent, while in other cases it may be a striking symptom. I regret that I cannot supply an answer to this question. If anything I have said should stimulate the removal of inhibitions which may prevent any of you from devoting your attention to this problem, I shall be satisfied that *my* time to-night, if not yours, has not been spent in vain.

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Section of Psychiatry

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[*October* 12, 1937]

Physical Research in Psychiatry: With Notes on the Need for Research into Hereditary Factors and for a System of Pedigree-Keeping

PRESIDENT'S ADDRESS

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THE advantage of Bethlem Royal Hospital when I was clinical assistant there for a year in the late eighties was the fine clinical material. The present material should be even more favourable (Mental Treatment Act, 1930). Patients were mainly of the early recoverable type, of a higher social and educational level than at public mental hospitals. The recovery-rate then was nearly 42% of the admissions; in 1936, between 38 and 39%. Taking three further years adjoining each of the two periods, the same general comparison obtains, as far as the respective methods of statement permit. The comparison is not surprising, since in the interim we have, in my opinion, made no advance in our knowledge of the pathogenesis of the psychoses. Consequently none in logical methods of treatment: the advance in the special case of dementia paralytica is not logical. There have been no brilliant flashes of empirical treatment to illuminate the dark firmament of psychiatry, unless shock—and seizure methods prove to be such. Prolonged sleep, as by somnifaine, is a gain. We were slow to try this, as is our custom. On the Continent they are more venturesome: more ready to take a risk. Do patients now get well sooner in recoverable psychoses? This has not been proved. Relapses in mania-melancholia have neither been cut down in number nor cut short, that I know of. This, if so, is a reproach. Instead of real knowledge we have had throughout the years a surfeit of terminological amplification and elaboration. The maze of classification + terminology has a perpetual fascination—an unproductive wandering, this—a measure of the difficulty of pathogenesis. More and more shall we leave the beaten track and wander in the bush of biochemistry and biophysics, hoping to come to grips with the problem of pathogenesis.

What shall we say about the failure to advance in the years that have passed, in the matter of the study of human genetics in general and the heredity of the psychoses and psychoneuroses in particular? About this, we in this country have done next to nothing until the last few years. In recent times the last-mentioned part of the subject has received attention abroad. The Genealogical Department of the German Research Institute in Psychiatry, Munich, has taken probably the foremost place. One has in mind the work of such men as Rüdin and Luxenburger. At present, for information based on extensive inquiry about such a subject as the outlook for the progeny where one or both parents have suffered from an attack of mental disorder, or one from such, the other being a psychopath, or for

[1] This address has been abbreviated.

information regarding the hereditary associations of such conditions as manic-depressive insanity or schizophrenia, we have to look abroad, especially, I consider, to Germany.

There are bodies here which lay themselves out to educate the public in matters appertaining to general and mental health; these deal with general and mental hygiene, antenatal care, child guidance, home and school influence, and the like. The subject of the environment has been riddled with the machine-guns of eloquence. How often do these mentors of the public, medical or other, touch upon the fundamentals of genetics, upon inheritance, and its bearing upon health and disease in the individual and his offspring? They take the line of least resistance, the environment, a subject lending itself to diffuse, uncritical platform oratory. I suspect that our social guides know exceedingly little about, and exhibit no enthusiasm to learn about, the hereditary factor. I would refer them to such a work as that by Frhr. v. Verschuer, of the Kaiser Wilhelm Institute for Anthropology, Human Heredity and Eugenics, Berlin-Dahlem, from which they will appreciate that more and more does the importance of the hereditary factor, from comparatively trivial to serious disease, thrust itself upon us. Even the members of our own profession seem to me to be in the main singularly uninterested and uninstructed in this matter. They cannot afford to be so much longer.

In no branch of medicine is this subject of inheritance more in need of attention than in that of so-called "psychological medicine": a pretentious term, which I dislike. Be it remembered that we are concerned by no means only with the matter of inheritance of the psychoses and psychoneuroses as such, but also with that of diseases which we know to be correlated with them or which systematic pedigree-keeping may show to be so. I find there is the same unreliable, incomplete, based-on-hearsay procedure of history-taking in vogue as was practised in those far-off days at Bethlem, and during my lengthy service. What we have to do is not to pander further to hearsay and memory, to choice between telling the truth and perverting or suppressing it, but to secure the facts by dealing with determination with the matter of pedigree-keeping. In recent times social service workers have been appointed at our best institutions for mental disorders. These are the people, after due instruction, to spread the gospel of the pedigree, and who should be supplied with a suitable pedigree-keeping schedule, for the purpose of instructing the responsible member of the families they visit.

In the late eighties and early nineties there were, in addition to Bethlem, two outstanding psychiatric institutions, the Royal Edinburgh Asylum and the West Riding Asylum, Wakefield. At the latter I was privileged to work as pathologist under Bevan Lewis, an outstanding figure in scientific psychiatry. The laboratory research work at Wakefield in the early nineties was, as it was bound to be at that time, concerned mainly with morbid anatomy and histology. In the latter Bevan Lewis was a leading exponent, whether in this country or abroad. By his method of staining ether-frozen, fresh brain sections of cortex cerebri by aniline blue-black the cells he called "scavenger" were well shown. They would probably be called astrocytes now. The foreign inclusion-substances, apparently fatty, which they showed were regarded by Bevan Lewis as products of degeneration of nerve-cells, phagocytosed. The prevailing view is probably that neither astrocytes nor oligoglia are concerned in removal of waste, or products of degeneration, which function is reserved to the microglia of del Rio Hortega. But this matter is even now not finally settled, and we find a lipophagocytic function still ascribed to the astrocytes here and there in the literature. v. Braunmühl (1932), in a review of general advances in histo-pathology, refers to both astrocytes and oligoglia as taking part in phagocytosis, as well as microglia, in chronic degenerations. The views of the Spanish School as to the entirely different action of macro- and micro-glia are not borne out by experimental lesions in rabbits. Questions for years in dispute regarding the neuroglia remain

unanswered, despite all the work done. Bevan Lewis's work was, in this direction, pioneer. As far as my knowledge goes it is not yet known which of the various cells described—whether some or all—belong to the reticulo-endothelial system. Tronconi (1935) deals fully, on the basis of modern impregnation-methods, with the human neuroglia. This article is followed by an imposing bibliography, which goes to show the immense amount of work done on this single subject. It is again to be gathered that the functions of the cells differentiated (astro-, micro-, oligo-glia) are obscure. How the glial architecture is modified in the most frequent maladies affecting the nervous system remains for examination.

It was about those early nineties that Nissl's cell-stain, silver-impregnation methods, and Weigert's medullary stain came into use here. The histological examination of the brain in the insane, such as was done at Wakefield, was necessary preliminary work. I think it was well understood by the older workers in this field that they were concerned with showing, not causes, but the micro-structural changes, if any, resulting from the operation of unknown causes (still unknown). These end-results in essential tissues might be regarded, if lasting, as added causes, bearing a share in the disordered mental manifestations. This work went to show that in the acute psychoses there are in the brain uncharacteristic morbid changes. Whatever the essential pathological causes, we continue to look upon them, pending further research, as exogenous and endogenous toxic substances, working upon a soil prepared by inheritance, acting through physico-chemical changes, and producing thus disorder of function by way of the essential elements subserving mental processes. In respect of a disorder of slow growth, such as (particularly) systematized delusional insanity, pathogenesis is still unknown territory. It would be hard to find a more marked instance of the difficulty of our problem.

The testimony of histological work is that the causative factors of the psychoses do not act locally as regards the brain, whether macroscopically (lobe or lobes) or microscopically (layer or layers of cortex). It does not strike one as philosophical to expect they should. Recently Marcus (1936) has described characteristic areas of demyelination in the striatum, pallidum, and corona radiata, especially of the frontal and temporal lobes, in schizophrenia, findings stated to agree with those of Buscaino, Ferraro, and other authors. This would be of interest, if borne out, by reason of the clinical similarities between this disease and post-encephalitic psychoses. If, as stated by Claude, disease affecting the frontal lobes can alter the whole personality, and the physiology of the frontal pole plays a great part in psychical activity, we should expect evidence of disease in some psychotics in the area concerned. If this is physico-chemical without histological counterpart it will be an experience of a new order.

Whilst the histological changes in the psychoses as a whole are not localized or characteristic (more recent work with improved methods bearing out the older work), the plaques and neuro-fibrillar changes in senile dementia, and especially the pre-senile dementia named after Alzheimer, are characteristic though not localized, except in the grey matter of the cerebrum. In Pick's disease there is local atrophy described as particularly present in the frontal and temporal lobes (especially their basal aspect, H. Spatz), and in these, atrophy of certain areas, even a concentration of such in the outer layers. B. Kihn (1932) refers to the need for study and elaboration of vital methods as applied to the histology of the nervous system, more particularly that of tissue-transplantation and culture. We know, he says, nothing as to the physical or physico-chemical nature of the breakdown-products of cells which we call neutral fat. The purpose of this article is to show the need for continued work on the problems of histological technique, in respect of nerve-cells, neuro-fibrils, axis-cylinders, and glia. This should be a wholesome corrective to the general neglect of histology in mental hospitals in this country nowadays.

Judging from publications, biochemical work in connexion with mental disorders

is still only prosecuted at quite a few laboratories, whether here or abroad, such as that at Cardiff (one of the first and of the foremost), the Deutsche Forschungs Anstalt at Munich, and the Psychiatric Institute and Hospital, New York. The shorter experience we have of biochemical and biophysical research, the restricted knowledge in these spheres, make it difficult to frame lines of research in consultation with those trained in the methods. We need to learn what is feasible, how far it is at present technically possible to carry out investigations which might suggest themselves to workers in medicine. Up to the present oxidation-processes of nerve-cells have probably claimed most attention, especially at Cardiff. The inhibitive influence of narcotic drugs and basic amines on normal oxidation (of glucose, lactic, and pyruvic acids) in the brain has been investigated. Narcotics have been shown to react with the tissue-enzymes, no permanent damage to the nerve-cells resulting. Damage done by the unknown morbid process in mania, melancholia, confusional states, benign stupor, must usually be reversible, since recovery occurs. The enzyme-activities are under investigation. The effect of such drugs as cocaine and mescalin, which cause hallucinations and other mental disturbances, on brain-oxidation, their mode of action, are matters for investigation. The detoxicating function of the liver likewise. With morbid disturbance of gastro-intestinal, renal, or liver-function, under the influence of various fevers and drugs, in states of disordered metabolism, we assume that toxic substances get access to the brain-cortex. We require to know what these are, and how they act. With provision for depuration of the cortex, is there a function of detoxication? The elaborate Danish work of H. Tómasson (1927) upon instability of ionic equilibrium in the serum in manic-depressive states, with its therapeutic indications, is in need of examination. The relationship of acid-base equilibrium and mental depression or the reverse should be investigated. Hoff (1936) produced what he describes as an acidotic state in himself and in two others, one a medical woman, by taking ammonium chloride for several days. During the "acid"-days depression resulted. He explains the depression of diabetic acidosis and of the pre-menstrual period, and at the onset of menstruation, on the basis of an acidosis then present. I doubt the value of isolated investigations of carbohydrates, lipoids, and mineral content of the blood, such as are reported: it would seem more reasonable to investigate the blood-chemistry as a whole in a given case.

Apart from functional investigations, which are more attractive, the chemical constitution of the different parts of the brain, at different ages, in man and allied animals, requires research, associated with like investigations in the psychoses and in mental defect. With reference to the matter of toxic action and the brain, katatonia, especially katatonic stupor, is to my mind suspect as regards a toxic origin, a view shared by many in various countries, especially since experience of metencephalitic states, with which there is much resemblance. The work done upon cases of this form of dementia præcox, in respect of disorders of function, goes to bear out this view. And much more of the same is required. The results obtained by bulbo-capnine should not be explained away by the statement that they are essentially different from those seen in katatonia and kataleptic states. Bulbo-capnine and cumarin (fluid extract of Tonka bean) produce psycho-somatic states showing great resemblance to conditions classed under "dementia præcox", e.g. torpor, excitability, katalepsy, katatonia, vasomotor disturbances. Such experimental investigations point to an organic and toxic causation of "dementia præcox" (admitting the hereditary foundation), constituting too valuable a clue to ignore.

The introduction of bacteriology at Wakefield about 1893 must have been one of the earliest applications of this subject to psychiatry in this country. We looked at our manias, melancholias, acute confusionals, our stupors, "anergic" and other, even our general paralytics, and they were good to look upon, for might they not be of bacterial (toxic) origin? Our talk was of exogenous, not endogenous toxins. Septic

foci, as possible pathological causes, were not within our ken, nor do I remember any reference to them as such in the literature of that time. Cases of functional disorder still looked, many of them, toxic in 1929, when I left the Cardiff Mental Hospital. But the horizon of toxic pathogenesis had widened. Meantime the claims of viruses, of disordered metabolism, of endogenous toxins generally, even in some cases, of septic foci, had obtruded themselves. All these remain in need of investigation. The work on septic foci has been mainly Anglo-American, and, as far as my reading goes, has not attracted much attention on the Continent. I agree with those who attribute to such foci but a limited rôle in pathogenesis.

The possible rôle of bacteria in mental disorders has been studied chiefly (as is natural) in connexion with intestinal organisms; in this country, mainly by the Ford-Robertsons (1929*a*, *b*), father and son, working chiefly with anaerobic organisms; by Shera, F. H. Stewart, Graves and Pickworth (septic foci); in Italy, by several workers, amongst whom Buscaino is prominent, who, in his monograph of 1932, gives the literature. He deals with bacteriological research demonstrating grave abnormalities of the intestinal flora in dementia præcox. The data recorded are based upon clinical, serological, X-ray, and bacteriological observations. The Ford-Robertsons have maintained the neurotoxic thesis. As recently as 1936 the effects on dogs and rabbits—katatonic bodily and mental symptoms—of injection of a neurotoxin from *B. coli* were described by Poppi (1936). The derivatives of the amino-acids, tyrosine, tryptophane, and histidine, are regarded as acting as toxins unless detoxicated in the liver. I would refer to work by F. H. Stewart (1929), with references to some of the literature; also to a paper by S. A. Mann and H. L. Shipp, from the Maudsley Laboratory, upon urinary reactions in relation to intestinal toxæmia in psychotics. Auto-intoxication in the psychoses and its causative agents are obscurities still as great as at the beginning of my experience.

I may here touch upon the relationship between skin-disorders and the nervous system. There is a very considerable literature, much of it given in an article by Marchionini (1934). Such conditions as eczema, urticaria, pruritus, erythromelalgia, sclerodermia, Raynaud's disease, alopecia areata are concerned. In several skin-disorders there is believed to be a so-called psychical origin, and instances of cure by psycho-therapy, suggestion, and hypnosis are recorded. The pathogenesis is obscure. Parts in the drama are assigned to the vegetative nervous system and endocrines, but this is mostly speculation. I am curious to know what the experience of those who deal with borderland states in the psychoneuroses is as regards association of these states and skin-disorders; it may be that the neurologist sees more of these disorders. From personal experience of mental hospital and psychiatric out-patient practice, and a study of psychiatric literature over many years, I should say that the absence of skin-disorders is the point to be noted. Yet many of these cases are amongst the " vegetative-stigmatized ". We have not, in my view, as yet been helped in psychiatry by the study of the hypophysis cerebri or any of the glands of internal secretion. Such has been undertaken chiefly in cases of dementia præcox. Their morbid histology and patho-physiology in the various psychoses are still matters for investigation.

There has, I consider, been far too little skilled inquiry, and far too few records of the state of the internal organs as a whole, as ascertained at autopsy, in mental hospitals, controlled by similar inquiry and records in general hospitals. Attention has been concentrated on the brain. This is mainly due to the absence of a whole-time pathologist, who should be on the staff of all large and medium-sized mental hospitals, especially such serving a city with university and medical school. The diseased condition of the kidneys in many of the insane has been commented on for years. Space does not permit me to refer to work upon this subject and on that of pathological livers. The question arises how far these conditions are associated with intestinal toxæmia (*see* Shaw, B. H., and Sladden, A. F., and Shatz, H. A. (1934); Shera, A. G. (1931); and Stewart, F. H.—cited by Shera). With regard to disordered

liver-function as estimated by the usual tests, work has been done in Scandinavia, thus, by Lingjaerde, and Marthuisen (1932), who cites supporting work. The former, borne out by the latter, finds liver-disorders in a very large proportion of schizophrenics in the active stage. This appears to connote the katatonic condition, especially katatonic stupor. The like evidence is found in the depressed form of mania-melancholia. The problem involves the consideration of gastro-intestinal disturbance. These observations need amplification and the support of microscopic examination.

Evidence of failure of the detoxicating function of the liver would be valuable, in view of the results of biochemical work by Quastel and Wheatley at Cardiff Mental Hospital upon brain-cell oxidation. I have in mind the possible interference with this by toxic substances absorbed from the gastro-intestinal tract. Buscaino, in his monograph referred to above, makes reference to a previous work (1923), in which he describes alterations in the liver and small intestines (organic, in the wall) in, amongst other brain-affections, cases of dementia præcox. The small intestine is only cut open in my experience for quite exceptional reasons at mental hospitals.

In the deplorable absence of University Psychiatric Clinics, with research departments, in this country—a reproach to British psychiatry—we have had to content ourselves with such research as can be done—apart from the special case of the Maudsley Hospital—in our public mental hospitals, registered hospitals for mental disorder, and mental defective institutions. Since the bulk of such work on the Continent has been done at the Neuro-psychiatric University Clinics, and not at the institutions corresponding with our mental hospitals, it is certain that we have not contributed our due share, for it is idle to maintain that our institutions have made up, or could make up, the difference. Now that the Mental Treatment Act 1930 permits of the reception of quite early cases into mental hospitals, and out-patient clinics are multiplying, the position is better as regards material for research. My fear is that these developments may act as a soporific, and hinder the establishment of the indispensable University Clinics.

The Board of Control (England and Wales) has for many years published in its Annual Reports an account of "Research and other Scientific Work" at the institutions which it supervises. That for 1935 states that the number of communications received has reached 76 as against 22 ten years ago. A study of these over a period of years shows that a considerable number of institutions make no return; that from many the return refers merely to routine laboratory work, or to work on dysentery or typhoid, or connected with tests and treatment in general paralysis. Only from a very few places is work worthy the name of research reported, and these remain much the same year after year. The conclusion is that the majority of these institutions are inadequately equipped with men and plant, and are without experimental licences, to do serious research work, whether clinical or laboratory. Nothing could illustrate more forcefully the need for the clinics with research departments referred to.

It is of interest that the heading "Genetics, History, After-history" appears first in the Board's Report for 1933, but returns under this heading were received from only three institutions; in 1934 from two; in 1935 from three. Which shows our backwardness in this, taking the long view, most important investigation of all. This is a line of research which practically all the numerous institutions concerned could follow. It is not a question of expensive plant here. Some training in procedure, and statistical advice in dealing with procedure and results are necessary; otherwise efforts will be wasted.

I am of opinion that the psychotic and defective should be examined by some approved scheme for ascertaining stigmata of degeneration, by measurement and observation. It is not enough to note that this or that psychotic or psychoneurotic has an abnormality of the ear, palate, digits, or the like. How would paranoiacs,

cases of confusional insanity, of anxiety-neuroses, hysteria, or epilepsy come out under such schematic examination? It would give us information regarding relative frequency of occurrence, and associated occurrence, of inborn abnormalities and, in connexion with family pedigrees, throw light on transmissibility, and desirability of avoidance of transmission, of abnormalities.

Reference to pyreto-therapy in the Reports of the Board of Control, which, whether in the form of drug, diathermy, or recent improvements in allied methods of causing high temperature, or vaccines, has not yet produced satisfactory results, brings to mind the disappointment many of us have experienced from the failure to find, over the last forty years, a safe and effective method, based upon the induction of fever, for promoting recovery or amelioration in such forms of insanity as mania, melancholia, stupor, acute confusion. A method comparable in effectiveness to acute intercurrent disease, such as influenza, pneumonia, cellulitis, erysipelas. I said "based upon the induction of fever": we have the empirical aim of producing a high temperature but are not absolved from the task of endeavouring to ascertain what the actual process is that brings about a favourable result. All these years, and no doubt longer, the remarkable curative or ameliorative effect of the above or other intercurrent maladies upon the psychoses has been known. Apart from the special instance of dementia paralytica, and the malarial treatment thereof, our efforts to copy Nature have failed, or at best produce temporary and partial results. On the one hand are exogenous toxins (various infective fevers) which produce psychoses, on the other the like which cure or improve them; unless, indeed, it is the febrile process which does this. We are still ignorant of the *modus operandi* of cure. This is an interesting field for research: as far as my knowledge goes it has not received sufficient attention, here or abroad. As regards the mode of action of malaria in dementia paralytica, this, I believe, has been investigated at the Maudsley Hospital. I have not the precise reference, but the article appeared in the *Journal of Mental Science* about June 1936. And also by T. v. Lehoczky (1935). From these two articles it is to be gathered that there is no evidence of formation of spirochæticidal bodies in malaria (no evidence of specific defence-mechanism), or evidence of disappearance of spirochætes by phagocytosis. The view of v. Lehoczky is that by pyrexial treatment in general the defensive mechanisms of the whole organism are mobilized. This shows that further research is needed, a view fortified by the consideration that malarial treatment of general paralysis is at times beneficial when the fever, as judged by temperature, is but slight. It remains to be seen whether the considerable pyrexia now obtainable by high-frequency methods is as effective in general paralysis and in mental disorders as are malarial treatment and intercurrent maladies.

Since university psychiatric clinics, with research facilities and team-work, will never absorb all cases susceptible of treatment, it behoves mental hospitals to apply to their (nowadays) more promising material, in the increasing measure of our knowledge, not only the routine-methods of clinical examination, but also tests of physiological function. Dr. Muriel Northcote (1932), working at the Cardiff Mental Hospital, published an article, "Somatic Changes in the Psychoses: A comprehensive investigation of the bodily functions of 30 psychotic patients, by means of clinical, pathological, biochemical, pharmacological, and radiological methods". Such work, progressively fortified by growth of knowledge and technique, is very necessary. A correlation between psychoses in the earliest available stages, and psychoneuroses, and performance of bodily function; cases of ascertained disease of any organ being excluded as far as possible. With regard to findings, Dr. Northcote refers to "a number of small deviations from the normal" and to "the large proportion of minor abnormalities" as being "not without significance". The slight abnormalities found indicate, she says, "a certain amount of upset of the various somatic functions, the true significance of which must await future research with improved and more delicate

methods". Deviations from the normal are also recorded by Hoskins (1933), who, in his research on schizophrenia, found variability above the normal in a large number of reactions. Considerable variation in the volume of urine was observed by Dr. Northcote; nearly one-half of the twenty-four-hour specimens examined were outside limits given as average, a large part being passed at night. This has been commented on by our medical and chemical staff, and clinical laboratory assistant, at Cardiff in the course of various researches: twenty-four-hour specimens, and the patients on a fixed diet. Some error in water-metabolism is suggested; Bumke, in his "Lehrbuch der Geisteskrankheiten", refers, under schizophrenia, to lesser changes of weight as associated with irregularities of water-metabolism. There is sudden, large secretion of urine. F. H. Sleeper (1934–35) made a careful study of urine-output in this condition. Omitting details, the average twenty-four-hour output of the patients was 2,532 c.c., as against 1,328 c.c. for the controls. Hoskins, cited above, conducted a five-year research on different bodily functions in a large number of schizophreniacs. He finds the average volume of urine to be twice as great as that of normal controls.

Disturbance in function of the autonomic nervous system is shown by various psychotics, especially perhaps by the stuporose-kataleptic—katatonic: such as œdema, acrocyanosis, with cold extremities, alterations in sweat—and sebum-secretion, abnormalities of heart-beat frequency, pupillary changes. In these types especially slight febrile movements and subnormal temperatures are described. In them, indeed, the symptoms and signs make an organic or toxic origin very probable, as already mentioned. In chronic encephalitis similar evidence of affection of the vegetative nervous system is found. I have a note of a statement by Bonhoeffer, whose work on the psychoses of infection is well known, that there is not one katatonic symptom which is not found in infection-psychoses. According to Bumke, most of the new schizophreniacs admitted for treatment in Germany in 1918–19 were received with the statement that the disorder originated in influenza. In the eighth Maudsley Lecture, 1927, summarizing, I stated that "these apparent anomalies of protein-metabolism, shown by this study of blood-plasma, cerebrospinal fluid and urine, can at present merely be recorded. Folin, it will be remembered, found abnormalities of metabolism in his classical study of the urine of the insane". In both these investigations (the other being Dr. Northcote's) at Cardiff, the patients were on a definite diet of known calorific value. In keeping with this argument, with examples, for the investigation of physiological function in the psychoses and psychoneuroses, are the findings of R. Gjessing (1932), of Oslo, a result of a most painstaking research, which I doubt has received sufficient attention in this country. This work is concerned with the patho-physiology of katatonic stupor. Space forbids details; I can merely say that a correlation between psychical state and somatic function is shown by these investigations.

The question or criticism is, I apprehend, inescapable, whether or not these and like and even more refined instances of disturbance of function are the cause of the mental symptoms observed. Some are content in the faith that somatic disorders are sometimes or often what they call of "psychical" or "psychogenetic" origin. This explanation is meaningless, and would appear to imply a misty belief in the operation of some occult, incomprehensible agency, something beyond our ken: the spirit or soul of the ecclesiastics. One hears the clergy speaking with assurance of body, mind, and spirit—a baffling trinity. But apart from such metaphysical indulgence there is, of course, the reaction of mind to mind, from which, therapeutically, good or evil may result. We cannot attempt more than the tracing of the physical reactions from sense-receptive organ onward, reactions involving both parties. The "mind-to-mind" mode of therapy is just another example of the empirical methods that we in medicine all employ at one time or another, or shall I say, most of the time? In my opinion we have no concern with lulling, seductive,

ætiological terms, in which the Greek language is so rich, such as " psychical " and " psychogenetic ". With the ertswhile " idiopathic " I should like to see them dropped. " Unknown " is humbler, and will do. Our affair is to perfect physical means of investigation, including experimental means, and study the physico-chemical substances involved. Not otherwise than (to employ Maudsley's style) the electrician or chemist investigates the forces he deals with up to a point, beyond which he cannot go.

The following are salient results of an inquiry directed to mental institutions and consultants on a suggestion I made to the sub-committee of the National Council of Mental Hygiene concerned. *Manic-depressive psychoses :* Can recovery be brought about or promoted ? Forty out of fifty replied in the affirmative. The means were the general measures commonly used. Also, removal of septic foci, colonic lavage, thyroid (in melancholia), pyreto-therapy, twilight sleep ; psycho-therapy. Can relapse be prevented ? Twenty-five out of fifty replied in the affirmative. The means were general. Seven replied, by psycho-analysis and therapy. Sir Maurice Craig considered that 5 gr. of medinal nightly keeps some well for many years and renders attacks less severe in others. There should be ample statistical information in mental institutions regarding frequency of relapse in individual patients, and the length of intermediate periods, yet but little has been published here. G. Fuller (1935) finds in the United States that of 327 cases of manic-depressive insanity 47·7% had been readmitted one or more times within the observation-period of ten years. We should certainly seek to prevent an appreciable amount of this relapsing, and I do not believe it cannot be done. When it comes to evidence of disturbance of physiological function in cases about to relapse, and whether means of treatment were based on research, the poverty of the information elicited by our questions is particularly apparent, and impresses one with the need for skilled attention to these matters.

In a Research Institute for Psychiatry—preferably, Neuro-Psychiatry—with clinic in connexion, the whole at a University centre with a medical school, we require to have available workers in the different branches of medicine and its basal sciences. The actual departments of the institute might be set out thus : *Genetics :* of the disorders concerned and those regarded as allied, or shown to be so by study ; *Normal and Pathological Physiology ; Normal and Morbid Anatomy ; Biochemistry and Biophysics ; Pharmacology and Therapeutics.*

The bulk of our psychopathic material is dealt with by the mental hospital services of the local authorities. Co-ordination and uniform control are in my view needed in their areas, so as to get a comprehensive grip of this material, in order to do our best for patients, but above all to promote prevention of psychopathy. In this latter sphere everything remains to be done. Our information about this material should be complete, embracing all social classes in a totalitarian grip. Early in 1936 I advocated a Director of Mental Health for each local authority or combination of authorities. Responsible as regards information, administration, disposal and supervision for all psychopathy in the area, and armed with authority to obtain from all concerned information for this purpose ; under him a department for human genetics. Pedigree-keeping (record of health, disease, defect, and cause of death, personal and family, as well as usual pedigree-particulars) to be compulsory, on a national scheme, with uniform pedigree-schedule—blank chart, specimen pedigree, symbols, explanatory notes. Such a scheme I outlined in 1936.

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